CONTENTS

General, physical, and inorganic

NO.		PAGE
427	Water-soluble complexes of niobium (columbium) and tantalum. Part II. The dissolution of niobic and tantalic acids in amine solutions By FRED FAIRBROTHER, DEREK ROBINSON, and JOHN B. TAYLOR	2074
429	The synthesis of derivatives of 1 : 4-diphenyldiethylenediphosphine By CHRISTOPHER H. S. HITCHCOCK and FREDERICK G. MANN	2081
431	The conductances of some chlorides in ethanol. Part I. Hydrochloric acid, cæsium chloride, magnesium chloride, and lanthanum chloride By A. M. EL-AGGAN, D. C. BRADLEY, and W. WARDLAW	2092
432	Solubility and heat of solution of 2 : 4 : 6-trinitrotoluene in sulphuric acid at 25° By B. J. KIRKBRIDE and P. A. H. WYATT	2100
433	The system CaO–Al_2O_3–H_2O at 5° By F. G. BUTTLER and H. F. W. TAYLOR	2103
441	The oxidation of the trisdipyridylosmium(II) ion by the peroxydisulphate ion in aqueous solution By D. H. IRVINE	2166
442	Higher complex fluorides of tungsten By G. B. HARGREAVES and R. D. PEACOCK	2170
455	Electrical conductances of solutions in nitric acid. Part II. Solutions of alkali-metal nitrates. Transport numbers and ionic conductances of NH_4^+, K^+, NO_2^+, and NO_3^- ions By W. H. LEE and D. J. MILLEN	2248
459	The action of two antibacterial agents on the growth of *Bact. lactis aerogenes* By B. J. MCCARTHY and SIR CYRIL HINSHELWOOD	2269
461	Metal carbonyl compounds. Part IV. An infrared spectroscopic investigation of some platinum(II) and palladium(II) carbonyl compounds By R. J. IRVING and E. A. MAGNUSSON	2283
468	Platinum(0) compounds with triarylphosphines and analogous ligands By L. MALATESTA and (MISS) C. CARIELLO	2323
470	Substituted benzidines and related compounds as reagents in analytical chemistry. Part XIV. 3-Bromo- and 3 : 3′-dibromo-benzidine as redox indicators By R. BELCHER, A. J. NUTTEN, and W. I. STEPHEN	2336
474	Peroxides of elements other than carbon. Part II. The formation of boron peroxides by nucleophilic substitution By ALWYN G. DAVIES and R. B. MOODIE	2372
475	Kinetics, mechanism, and chemistry of the thermal decomposition of ammonium dichromate By JOHN SIMPSON, DUNCAN TAYLOR, and (in part) D. M. W. ANDERSON	2378
481	Infrared spectra of boron compounds By L. J. BELLAMY, W. GERRARD, M. F. LAPPERT, and R. L. WILLIAMS	2412
	NOTES	
482	Nitrous acid equilibria in perchloric acid By T. A. TURNEY and G. A. WRIGHT	2415
487	The oxyfluorides of manganese and iodine By E. E. AYNSLEY	2425
490	Pyrolysis of phenylmercuric iodide By M. COWPERTHWAITE and E. WARHURST	2429
493	Trismethylmercurisulphonium nitrate and dichromate By D. GRDENIĆ and B. MARKUŠIĆ	2434

XUM

Physical organic

NO.		PAGE
436	Stages in oxidations of organic compounds by potassium permanganate. Part IX. Oxidation of allyl alcohol by manganic pyrophosphate By HARING LAND and WILLIAM A. WATERS	2129
443	Chemical action of ionising radiations in solution. Part XXI. The action of ^{60}Co γ-radiation on aqueous solutions of ethylene at different pressures By P. G. CLAY, G. R. A. JOHNSON, and J. WEISS	2175
444	*N*-Oxides and related compounds. Part XII. Infrared spectra of some carbonyl compounds By A. R. KATRITZKY, A. M. MONRO, and (in part) J. A. T. BEARD, D. P. DEARNALEY, and N. J. EARL	2182
445	*N*-Oxides and related compounds. Part XIII. Infrared spectra of 4-substituted pyridine 1-oxides By A. R. KATRITZKY and J. N. GARDNER	2192
446	*N*-Oxides and related compounds. Part XIV. Infrared spectra of 2-substituted pyridine 1-oxides By A. R. KATRITZKY and A. R. HANDS	2195
447	Infrared studies of heterocyclic compounds. Part I. 4-Substituted pyridines By A. R. KATRITZKY and J. N. GARDNER	2198
448	Infrared studies of heterocyclic compounds. Part II. 2-Monosubstituted pyridines By A. R. KATRITZKY and A. R. HANDS	2202
456	The mechanisms of inhibition and retardation in radical polymerizations. Part IV. The effects of diphenylpicrylhydrazine and a condensation product of acetone with phenylhydroxylamine upon the sensitized polymerization of styrene By J. C. BEVINGTON and N. A. GHANEM	2254
458	The solvolysis of acetic anhydride in 50% aqueous acetone catalysed by nitrite ion By E. B. LEES and B. SAVILLE	2262
469	The acid–base function in non-aqueous solution. Part I. The equilibria between mono-, di-, or tri-*n*-butylamine and 2 : 4-dinitrophenol in chlorobenzene By JOHN W. BAYLES and A. CHETWYN	2328
471	The structure of molecular compounds. Part XII. Molecular compounds of tri-*o*-thymotide By D. LAWTON and H. M. POWELL	2339
473	Flavan derivatives. Part I. The absolute configuration of (+)-dihydroquercetin By J. W. CLARK-LEWIS and W. KORYTNYK	2367
479	Anionotropic systems. Part V. A kinetic investigation of the rearrangement of 1-phenylallyl esters in non-aqueous solvents By (the late) E. A. BRAUDE, D. W. TURNER, and E. S. WAIGHT.	2396
480	Anionotropic systems. Part VI. The rearrangement of 1-phenylallyl *p*-nitrobenzoate in chlorobenzene. Tracer studies By (the late) E. A. BRAUDE and D. W. TURNER	2404
NOTE		
484	Oxygen exchange between nitric acid and water. Part IV. The nitration of 2-mesitylethanesulphonic acid By C. A. BUNTON and G. STEDMAN	2420

Organic

426	The configuration of adrenaline and of its *p*-hydroxyphenyl analogue By P. PRATESI, A. LA MANNA, A. CAMPIGLIO, and V. GHIZLANDI	2069
428	5-Methoxy-*N*-methyltryptamine: a new indole alkaloid from *Phalaris arundinacea* L. By S. WILKINSON	2079
430	Cyclic amidines. Part VII. Preparation of benziminazoles from *N'*-aryl-*N*-hydroxyamidines By M. W. PARTRIDGE and H. A. TURNER	2086

NO.		PAGE
434	Alicyclic glycols. Part XVI. Decalin 2 : 3-ketols By MD. ERFAN ALI and L. N. OWEN	2111
435	Alicyclic glycols. Part XVII. The decalin-2 : 3-diols By MD. ERFAN ALI and L. N. OWEN	2119
437	Derivatives of acetoacetic acid. Part IX. The reaction of diketen with carbodiimides By R. N. LACEY and W. R. WARD	2134
438	Bisbenzyl*iso*quinolines. Part II. The synthesis of 5-(2-aminoethyl)-4′-carboxy-2 : 3-dimethoxydiphenyl ether By J. R. CROWDER, M. F. GRUNDON, and J. R. LEWIS	2142
439	The preparation and donor properties of some silylamines By E. A. V. EBSWORTH and H. J. EMELÉUS	2150
440	Studies in the steroid group. Part LXXI. The preparation and reactions of 9α-methylergostane derivatives By E. R. H. JONES, G. D. MEAKINS, and J. S. STEPHENSON	2156
449	Reactions of unsaturated compounds. Part XIV. The oxidation of 2 : 2 : 4 : 6 : 6-pentamethylhept-3-ene By M. A. DAVIS and W. J. HICKINBOTTOM	2205
450	Stereochemical investigations of cyclic bases. Part II. Hofmann degradation of some cyclic quaternary ammonium salts By K. JEWERS and J. MCKENNA	2209
451	Amino-sugars and related compounds. Part IV. Isolation and properties of oligosaccharides obtained by controlled fragmentation of chitin By S. A. BARKER, A. B. FOSTER, M. STACEY, and J. M. WEBBER	2218
452	Metallation and carboxylation of chrysene By S. E. HUNT and A. S. LINDSEY	2227
453	Bergenin, a *C*-glycopyranosyl derivative of 4-*O*-methylgallic acid By J. EVELYN HAY and L. J. HAYNES	2231
454	Triterpenoids. Part XXIV. Further investigations on the constitution of zeorin By D. H. R. BARTON, P. DE MAYO, and J. C. ORR	2239
457	Organic fluorine compounds. Part IX. The preparation of fluoroacetone and 1 : 3-difluoroacetone By ERNST D. BERGMANN and SASSON COHEN	2259
460	Chalcones and related compounds. Part V. Addition of nitro-compounds to chalcones By W. DAVEY and D. J. TIVEY	2276
462	Reactions of organic peroxides. Part IX. Hydroperoxides of some alkyltetralins By B. YEOMANS and DONALD P. YOUNG	2288
463	Purines, pyrimidines, and glyoxalines. Part IX. Syntheses of uridine, 2-thiouridine, and some related compounds By G. SHAW, R. N. WARRENER, and (in part) (MISS) M. H. MAGUIRE and R. K. RALPH	2294
464	Purines, pyrimidines, and glyoxalines. Part X. Synthesis of uracil-6-phosphonic acid, an analogue of orotic acid By (MISS) M. H. MAGUIRE, R. K. RALPH, and G. SHAW	2299
465	Synthetic and stereochemical investigations of reduced cyclic bases. Part V. The exhaustive methylation of some partially reduced cyclic bases By H. BOOTH, F. E. KING, and J. PARRICK	2302
466	Experiments on the synthesis of substances related to the sterols. Part LIV. Degradative and synthetical studies on the A-ring of androst-4-ene-3 : 17-dione By M. J. TEMPLE ROBINSON	2311
467	The stereochemistry of some 1 : 5-diaza*cyclo*octane derivatives By R. KOLIŃSKI, (MISS) H. PIOTROWSKA, and T. URBAŃSKI	2319
472	Structure of the capsular polysaccharide of *Aerobacter aerogenes* (N.C.T.C. 418) By S. A. BARKER, A. B. FOSTER, I. R. SIDDIQUI, and M. STACEY	2358

NO. PAGE

476 The mechanism of *N*-acylation of 2-mercaptoglyoxalines
By J. A. BAKER 2387

477 The preparation and analytical properties of *NN*-di(carboxymethyl)aminomethyl derivatives of some hydroxyanthraquinones
By R. BELCHER, M. A. LEONARD, and T. S. WEST 2390

478 Submicro-methods for the analysis of organic compounds. Part III. Determination of *N*-methyl groups and the simultaneous determination of alkoxyl and *N*-methyl groups
By R. BELCHER, M. K. BHATTY, and T. S. WEST 2393

NOTES

483 Thiophen derivatives. Part XII. Some derivatives of 2-ethylthiophen
By NG. PH. BUU-HOÏ 2418

485 Preparation of some naphthopyrans
By R. LIVINGSTONE, D. MILLER, and R. B. WATSON 2422

486 Reactions of amino-acids with acetic acid
By E. A. BELL 2423

488 5-Nitro- and 5-amino-2-benzylbenziminazole
By B. N. FEITELSON and R. ROTHSTEIN 2426

489 *m*-Hydrazinostyrene
By C. L. ARCUS and R. E. SCHAFFER 2428

491 The *C*-benzylation of phenols by use of sodium hydride
By F. M. ELKOBAISI and W. J. HICKINBOTTOM 2431

492 Alkaloids of *Rauwolfia* species. Part IV. *Rauwolfia cambodiana* Pierre
By D. A. A. KIDD 2432

494 The Hunsdiecker reaction in the pyrazole series
By E. G. BRAIN and I. L. FINAR 2435

INDEX OF AUTHORS' NAMES

ALI, Md. E., and Owen, L. N., 2111, 2119
Anderson, D. M. W. See Simpson, J., 2378
Arcus, C. L., and Schaffer, R. E., 2428
Aynsley, E. E., 2425
Baker, J. A., 2387
Barker, S. A., Foster, A. B., Siddiqui, I. R., and Stacey, M., 2358
Barker, S. A., Foster, A. B., Stacey, M., and Webber, J. M., 2218
Barton, D. H. R., de Mayo, P., and Orr, J. C., 2239
Bayles, J. W., and Chetwyn, A., 2328
Beard, J. A. T. See Katritzky, A. R., 2182
Belcher, R., Bhatty, M. K., and West, T. S., 2393
Belcher, R., Leonard, M. A., and West, T. S., 2390
Belcher, R., Nutten, A. J., and Stephen, W. I., 2336
Bell, E. A., 2423
Bellamy, L. J., Gerrard, W., Lappert, M. F., and Williams, R. L., 2412
Bergmann, E. D., and Cohen, S., 2259
Bevington, J. C., and Ghanem, N. A., 2254
Bhatty, M. K. See Belcher, R., 2393
Booth, H., King, F. E., and Parrick, J., 2302
Bradley, D. C. See El-Aggan, A. M., 2092
Brain, E. G., and Finar, I. L., 2435
Braude, E. A., and Turner, D. W., 2404
Braude, E. A., Turner, D. W., and Waight, E. S., 2396
Bunton, C. A., and Stedman, G., 2420
Buttler, F. G., and Taylor, H. F. W., 2103
Buu-Hoï, Ng. Ph., 2418
Campiglio, A. See Pratesi, P., 2069
Cariello, C. See Malatesta, L., 2323
Chetwyn, A. See Bayles, J. W., 2328
Clark-Lewis, J. W., and Korytnyk, W., 2367
Clay, R. G., Johnson, G. R. A., and Weiss, J., 2175
Cohen, S. See Bergmann, E. D., 2259
Cowperthwaite, M., and Warhurst, E., 2429
Crowder, J. R., Grundon, M. F., and Lewis, J. R., 2142
Davey, W., and Tivey, D. J., 2276
Davies, Alwyn G., and Moodie, R. B., 2372
Davis, M. A., and Hickinbottom, W. J., 2205
Dearnaley, D. P. See Katritzky, A. R., 2182
de Mayo, P. See Barton, D. H. R., 2239
Earl, N. J. See Katritzky, A. R., 2182
Ebsworth, E. A. V., and Emeléus, H. J., 2150
El-Aggan, A. M., Bradley, D. C., and Wardlaw, W., 2092
Elkobaisi, F. M., and Hickinbottom, W. J., 2431
Emeléus, H. J. See Ebsworth, E. A. V., 2150
Fairbrother, F., Robinson, D., and Taylor, J. B., 2074
Feitelson, B. N., and Rothstein, R., 2426
Finar, I. L. See Brain, E. G., 2435
Foster, A. B. See Barker, S. A., 2218, 2358
Gardner, J. N. See Katritzky, A. R., 2192, 2198
Gerrard, W. See Bellamy, L. J., 2412
Ghanem, N. A. See Bevington, J. C., 2254
Ghislandi, V. See Pratesi, P., 2069
Grdenić, D., and Markušić, B., 2434
Grundon, M. F. See Crowder, J. R., 2142

Hands, A. R. See Katritzky, A. R., 2195, 2202
Hargreaves, G. B., and Peacock, R. D., 2170
Hay, J. E., and Haynes, L. J., 2231
Haynes, L. J. See Hay, J. E., 2231
Hickinbottom, W. J. See Davis, M. A., 2205, and Elkobaisi, F. M., 2431
Hinshelwood, Sir C. See McCarthy, B. J., 2269
Hitchcock, C. H. S., and Mann, F. G., 2081
Hunt, S. E., and Lindsey, A. S., 2227
Irvine, D. H., 2166
Irving, R. J., and Magnusson, E. A., 2283
Jewers, K., and McKenna, J., 2209
Johnson, G. R. A. See Clay, P. G., 2175
Jones, E. R. H., Meakins, G. D., and Stephenson, J. S., 2156
Katritzky, A. R., and Gardner, J. N., 2192, 2198
Katritzky, A. R., and Hands, A. R., 2195, 2202
Katritzky, A. R., Monro, A. M., Beard, J. A. T., Dearnaley, D. P., and Earl, N. J., 2182
Kidd, D. A. A., 2432
King, F. E. See Booth, H., 2302
Kirkbride, B. J., and Wyatt, P. A. H., 2100
Koliński, R., Piotrowska, H., and Urbański, T., 2319
Korytnyk, W. See Clark-Lewis, J. W., 2367
Lacey, R. N., and Ward, W. R., 2134
La Manna, A. See Pratesi, P., 2069
Land, H., and Waters, W. A., 2129
Lappert, M. F. See Bellamy, L. J., 2412
Lawton, D., and Powell, H. M., 2339
Lee, W. H., and Millen, D. J., 2248
Lees, E. B., and Saville, B., 2262
Leonard, M. A. See Belcher, R., 2390
Lewis, J. R. See Crowder, J. R., 2142
Lindsey, A. S. See Hunt, S. E., 2227
Livingstone, R., Miller, D., and Watson, R. B., 2422
McCarthy, B. J., and Hinshelwood, Sir C., 2269
McKenna, J. See Jewers, K., 2209
Magnusson, E. A. See Irving, R. J., 2283
Maguire, M. H., Ralph, R. K., and Shaw, G., 2299
Maguire, M. H. See also Shaw, G., 2294
Malatesta, L., and Cariello, C., 2323
Mann, F. G. See Hitchcock, C. H. S., 2081
Markušić, B. See Grdenić, D., 2434
Meakins, G. D. See Jones, E. R. H., 2156
Millen, D. J. See Lee, W. H., 2248
Miller, D. See Livingstone, R., 2422
Monro, A. M. See Katritzky, A. R., 2182
Moodie, R. B. See Davies, Alwyn G., 2372
Nutten, A. J. See Belcher, R., 2336
Orr, J. C. See Barton, D. H. R., 2239
Owen, L. N. See Ali, Md. E., 2111, 2119
Parrick, J. See Booth, H., 2302
Partridge, M. W., and Turner, H. A., 2086
Peacock, R. D. See Hargreaves, G. B., 2170
Piotrowska, H. See Koliński, R., 2319
Powell, H. M. See Lawton, D., 2339
Pratesi, P., La Manna, A., Campiglio, A., and Ghislandi, V., 2069
Ralph, R. K. See Maguire, M. H., 2299, and Shaw, G., 2294
Robinson, D. See Fairbrother, F., 2074
Robinson, M. J. T., 2311
Rothstein, R. See Feitelson, B. N., 2426
Saville, B. See Lees, E. B., 2262
Schaffer, R. E. See Arcus, C. L., 2428
Shaw, G., Warrener, R. N., Maguire, M. H., and Ralph, R. K., 2294
Shaw, G. See also Maguire, M. H., 2299
Siddiqui, I. R. See Barker, S. A., 2358
Simpson, J., Taylor, D., and Anderson, D. M. W., 2378
Stacey, M. See Barker, S. A., 2218, 2358
Stedman, G. See Bunton, C. A., 2420
Stephen, W. I. See Belcher, R., 2336
Stephenson, J. S. See Jones, E. R. H., 2156
Taylor, D. See Simpson, J., 2378
Taylor, H. F. W. See Buttler, F. G., 2103
Taylor, J. B. See Fairbrother, F., 2074
Tivey, D. J. See Davey, W., 2276
Turner, D. W. See Braude, E. A., 2396, 2404
Turner, H. A. See Partridge, M. W., 2086
Turney, T. A., and Wright, G. A., 2415
Urbański, T. See Koliński, R., 2319
Waight, E. S. See Braude, E. A., 2396
Ward, W. R. See Lacey, R. N., 2134
Wardlaw, W. See El-Aggan, A. M., 2092
Warhurst, E. See Cowperthwaite, M., 2429
Warrener, R. N. See Shaw, G., 2294
Waters, W. A. See Land, H., 2129
Watson, R. B. See Livingstone, R., 2422
Webber, J. M. See Barker, S. A., 2218
Weiss, J. See Clay, P. G., 2175
West, T. S. See Belcher, R., 2390, 2393
Wilkinson, S., 2079
Williams, R. L. See Bellamy, L. J., 2412
Wright, G. A. See Turney, T. A., 2415
Wyatt, P. A. H. See Kirkbride, B. J., 2100
Yeomans, B., and Young, D. P., 2288
Young, D. P. See Yeomans, B., 2288

PAPERS ACCEPTED

The basicity of thia-azetidines, dihydrodithiazines, and tetrahydrothiadiazines. By D. COLLINS and J. GRAYMORE

Cyclic organic boron compounds. Part I. Preparation, characterisation, and stability of esters of metaboric acid. By M. F. LAPPERT

New heteroaromatic compounds. Part I. 9-Azaboraphenanthrene. By M. J. S. DEWAR, VED. P. KUBBA, and R. PETTIT

New heteroaromatic compounds. Part II. Boron compounds *iso*conjugate with indole, 2 : 3-benzofuran, and thionaphthen. By M. J. S. DEWAR, VED. P. KUBBA, and R. PETTIT

Organic sulphur compounds. Part I. Action of organomagnesium haloids on diaroyl disulphides. By MOHAMED A. ELKASCHEF and MICHAEL H. NOSSEIR

Reduced cyclic compounds. Part V. The intramolecular acylation of some olefinic acids. By M. F. ANSELL and S. S. BROWN

The synthesis of kinetin and some related heterocyclic compounds. By R. HULL

The chemotherapy of schistosomiasis. Part I. Derivatives and analogues of αω-di-(*p*-aminophenoxy)alkanes. By J. N. ASHLEY, R. F. COLLINS, M. DAVIS, and N. E. SIRETT

The thermal decomposition of keten. By J. R. YOUNG

Steroids and Walden inversion. Part XLI. The configuration of the bromination products of 5α-androstan-17-one. By C. W. SHOPPEE, R. H. JENKINS, and G. H. R. SUMMERS

Vapour pressures of metal alkoxides. Part I. Titanium tetra-*tert.*-butoxide and -amyloxide. By D. C. BRADLEY and J. D. SWANICK

The synthesis of 6-dimethylamino-9-β-D-ribofuranosidopurine-5′ phosphate. By K. J. M. ANDREWS and W. E. BARBER

A detailed refinement of the crystal and molecular structure of thiourea. By N. R. KUNCHUR and MARY R. TRUTER

The constitution of complex metallic salts. Part XVIII. The chelated metallic derivatives of *NNN′N′*-tetramethylethylenediamine and of 1 : 4-dimethylpiperazine. By FREDERICK G. MANN and H. R. WATSON

Carcinogenic nitrogen compounds. Part XXV. Steric hindrance to cyclisation of 6-aminochrysene and its derivatives. By G. C. BARRETT and NG. PH. BUU-HOÏ

Sugar nitrates. Part V. Removal of nitrate groups. By K. S. ENNOR and JOHN HONEYMAN

Back-co-ordination from oxygen to boron in organoboron compounds. By E. W. ABEL, W. GERRARD, M. F. LAPPERT, and R. SHAFFERMAN

The ring-expansion of 3 : 4-benzofluorenone by hydrazoic acid. By B. R. T. KEENE and K. SCHOFIELD

Electrophilic substitution. Part XII. The nitration of diphenylmethane, fluorene, diphenyl ether, dibenzofuran, diphenylamine, and carbazole, relative reactivities and partial rate factors. By M. J. S. DEWAR and D. S. URCH

The titration and the apparent dissociation constants of weak acids in mixed aqueous solvents. By M. K. HARGREAVES and P. J. RICHARDSON

The kinetics and mechanisms of nucleophilic displacement in allylic systems. Part IX. Bimolecular substitution with rearrangement in the reaction of 1-*tert.*-butylallyl chloride with ethoxide ion. By P. B. D. DE LA MARE, E. D. HUGHES, P. C. MERRIMAN, L. PICHAT, and C. A. VERNON

Heteropoly-tungstic acids and heteropoly-tungstates. Part III. 12-Tungstozincic acid and its salts, and some 12-tungsto-3-zincates. By DONALD H. BROWN and JOHN A. MAIR

Chemical applications of nuclear quadrupole resonance spectroscopy. Part I. Some chloroderivatives of nitrogen heterocycles. By M. J. S. DEWAR and E. A. C. LUCKEN

Preparation and some crystallographic properties of triamminoacetylenemagnesium carbide, $MgC_2 \cdot C_2H_2 \cdot 3NH_3$. By E. L. LIPPERT and MARY R. TRUTER

Hexamethyl compounds of silicon, germanium, and tin. By M. P. BROWN and G. W. A. FOWLES

Cytotoxic compounds. Part I. *p-NN*-Di-2′-chloroethyl- and *p-NN*-di-2′-bromoethyl-aminothiophenol. By M. H. BENN, L. N. OWEN, and (in part) A. M. CREIGHTON

The preparation and properties of some plutonium compounds. Part VIII. Plutonium(IV) sulphate. By J. L. DRUMMOND and G. A. WELCH

Effect of various anions on thickness and active-oxygen content of nickel oxide layers formed by repeated anodic–cathodic cycling; the specific effect of chloride ions and its dependence on the nature of the substrate. By H. K. EMBABY and A. A. MOUSSA

XUM

The preparation of some esters of methyl 4 : 6-*O*-benzylidene-α-D-altroside. By K. S. Ennor, John Honeyman, C. J. G. Shaw, and Theo. C. Stening

New *NN'*-disubstituted thioureas and ureas of biological interest. By Ng. Ph. Buu-Hoï and Ng. D. Xuong

Stereochemical investigations of cyclic bases. Part III. An example of Wagner–Meerwein elimination with a quaternary ammonium salt. By J. McKenna and J. B. Slinger

Gibberellic acid. Part IX. The structure of *allo*gibberic acid. By T. P. C. Mulholland

Gibberellic acid. Part X. 7-Hydroxy-1-methylfluorene. By A. Morrison and T. P. C. Mulholland

Reactions and stability of chabazite-like phases. Part I. Ion-exchanged forms of natural chabazite. By R. M. Barrer and D. A. Langley

Reactions and stability of chabazite-like phases. Part II. Ion-exchanged forms of some synthetic species. By R. M. Barrer and D. M. Langley

Reactions and stability of chabazite-type phases. Part III. Intracrystalline water. By R. M. Barrer and D. A. Langley

Polycyclic systems. Part II. Synthesis of some chrysene and hydrochrysene derivatives. By D. Nasipuri, A. C. Chaudhuri, and J. Roy

Molecular polarisability. Application of the N–H and N–C link polarisabilities to the conformations of tertiary amines, piperidine, and morpholine. By M. Aroney and R. J. W. Le Fèvre

Glyoxalinopyrimidines. Part II. By J. Clark and G. R. Ramage

Griseofulvin. Part XIII. Homologues of griseofulvin and 7-chloro-4 : 6 : 4'-trimethoxy-6'-methylgris-3'-ene-3 : 2'-dione. By L. A. Duncanson, John Frederick Grove, and P. W. Jeffs

Condensations of the xylenols with carbon tetrahalides. By J. E. Driver and (Miss) T. F. Lai

Solvated triphenylmethane derivatives containing bromine. By J. E. Driver and (Miss) T. F. Lai

α-1 : 4-Glucosans. Part IX. The molecular structure of a starch-type polysaccharide from *Dunaliella biculata*. By B. P. Eddy, I. D. Fleming, and D. J. Manners

The phosphates of calcium. Part V. Revision of the earlier space diagram. By Henry Bassett

The reactions of methylene with *iso*butene. By J. H. Knox, A. F. Trotman-Dickenson, and C. H. J. Wells

Studies on phosphorylation. Part XVII. The hydrolysis of methyl 3-(*OO*-dimethylphosphoryloxy)but-2-enoate. By E. Y. Spencer, Sir Alexander Todd, and R. F. Webb

Diphenylenes. Part II. Syntheses of substituted diphenylenes and of related diphenyls. By Wilson Baker, J. W. Barton, and J. F. W. McOmie

Diphenylenes. Part III. Substitution in the nucleus. By Wilson Baker, J. W. Barton, and J. F. W. McOmie

Attempts to synthesise 1 : 2 : 3 : 4-tetrahydro-1 : 5-dihydroxy-6 : 8-dimethylnaphthalene-2-α-propionic lactone. By Wesley Cocker, T. B. H. McMurry, (Mrs.) L. Mabrouk, and W. R. M. Williamson

A new double spoon gauge. By J. D. Swanwick

Mannitol production by a *Lactobacillus* causing ropiness in cider. By S. A. Barker, E. J. Bourne, Elisabeth Salt, and M. Stacey

An exchange reaction of arenesulphenyl chlorides with organic disulphides. By C. G. Moore and M. Porter

Heterocyclic analogues of fluorene: indeno(1' : 2'-4 : 5)thiazoles from 2-bromoindan-1-one. By C. L. Arcus and G. C. Barrett

Hydrolysis of simple amides catalysed by carboxylic acids. By K. G. Wyness

The stereochemistry of arjunolic acid. By F. E. King, T. J. King, and J. D. White

The synthesis of *vic*-dioximes from symmetrical ketones. By R. Belcher, W. Hoyle, and T. S. West

The chemistry of triterpenes and related compounds. Part XXXIII. The isolation of ergosta-7 : 22-dien-3-one from *Fomes fomentarius*. By H. R. Arthur, T. G. Halsall, and R. D. Smith

The effect of conformation on the rate of unimolecular solvolysis of aralkyl chlorides. By G. Baddeley, J. W. Rasburn, and R. Rose

Relationship between hyperconjugation and conformation. Part II. The ethyl alcoholysis of some homologues of diphenylmethyl chloride. By G. Baddeley, S. Varma, and (in part) M. Gordon

Three iodides of rhenium. By R. D. Peacock, A. J. E. Welch, and L. F. Wilson

XUM

Deoxynucleosides and related compounds. Part VI. The synthesis of 2-thiouridine and of 3′-deoxyuridine. By D. M. Brown, D. B. Parihar, Sir Alexander Todd, and S. Varadarajan

Deoxynucleosides and related compounds. Part VII. The synthesis of 2′-deoxyuridine and of thymidine. By D. M. Brown, D. B. Parihar, C. B. Reese, and Sir Alexander Todd

Preparation of cyanamide. By Alexander Lawson and J. O. Stevens

Picrotoxin. Part VII. The chemistry of anhydropicrotin. By J. S. E. Holker, Alexander Robertson, J. H. Taylor, and (in part) K. U. Holker, and W. R. N. Williamson

A study of the deuteration of glyoxaline by nuclear magnetic resonance. By R. J. Gillespie, A. Grimison, J. H. Ridd, and R. F. H. White

Polarography of some aromatic carbonyl compounds in dimethylformamide. By P. H. Given, M. E. Peover, and J. Schoen

Polarographic reduction of carbonyl groups in solvent extracts of coals. By P. H. Given and J. Schoen

Polarography of conjugated systems in dimethylformamide. By P. H. Given

426. *The Configuration of Adrenaline and of its* p-*Hydroxyphenyl Analogue.*

By P. Pratesi, A. La Manna, A. Campiglio, and V. Ghislandi.

Reduction of optically active mandelamides by lithium aluminium hydride to the corresponding amines without appreciable racemisation permits deduction of the configuration of sympathomimetic amines from that of suitably substituted mandelic acids. In this way the configuration of adrenaline and of its *p*-hydroxyphenyl analogue has been correlated with that of the mandelic acid, through 3-amino-4-methoxy- and 4-hydroxymandelic acid. The configuration of D(−)-mandelic acid is found for natural lævorotatory adrenaline and its lævorotatory *p*-hydroxyphenyl analogue.

Knowledge of configurational relationships in the field of optically active sympathomimetic amines is an important element in interpreting and forecasting the specific biological properties of these bases. We here report a purely chemical determination of the configuration of adrenaline and its *p*-hydroxyphenyl analogue.

Freudenberg [1] suggested, but without experimental evidence, that (−)-adrenaline had configuration (I) by analogy with (−)-ephedrine and (−)-ψ-ephedrine whose steric configuration had been unambiguously established (all formulæ in this paper are Fischer projections). Blaschko, Holton, and Stanley [2] later found that Dalgliesh and Mann's racemic 3 : 4-dihydroxyphenylserine [3] was decarboxylated by an L-amino-acid decarboxylase from *Streptococcus faecalis* to (−)-noradrenaline in 50% yield; Dalgliesh [4] suggested that the serine used had the *erythro*-configuration and consequently that the configuration of adrenaline was the opposite of (I), basing this on the well-known biogenetic relation of noradrenaline to adrenaline. However, from infrared spectrophotometric studies Bolhofer [5] ascribed to the same substrate the *threo*-configuration, and Hartman, Pogrund, Drell, and Clark [6] showed that the other racemic form of 3 : 4-dihydroxyphenylserine, to which they ascribe the *erythro*-configuration, is enzymically decarboxylated to (+)-noradrenaline. Thus, Drell [7] reached the same conclusion as Freudenberg as to the configuration of natural adrenaline, but pointed out that the configuration of the *threo*-serine derivative is not unequivocally established, so that the configurational assignment for adrenaline is not definitive.

Reduction of optically active mandelamides by lithium aluminium hydride to the corresponding amines without appreciable racemisation,[8] makes it possible to deduce the configuration of sympathomimetic amines from that of suitably substituted mandelic acids. This method has now been applied to adrenaline. The chemical transformations were first carried out on the racemic compounds [9] and they have now been applied to the optically active substances.

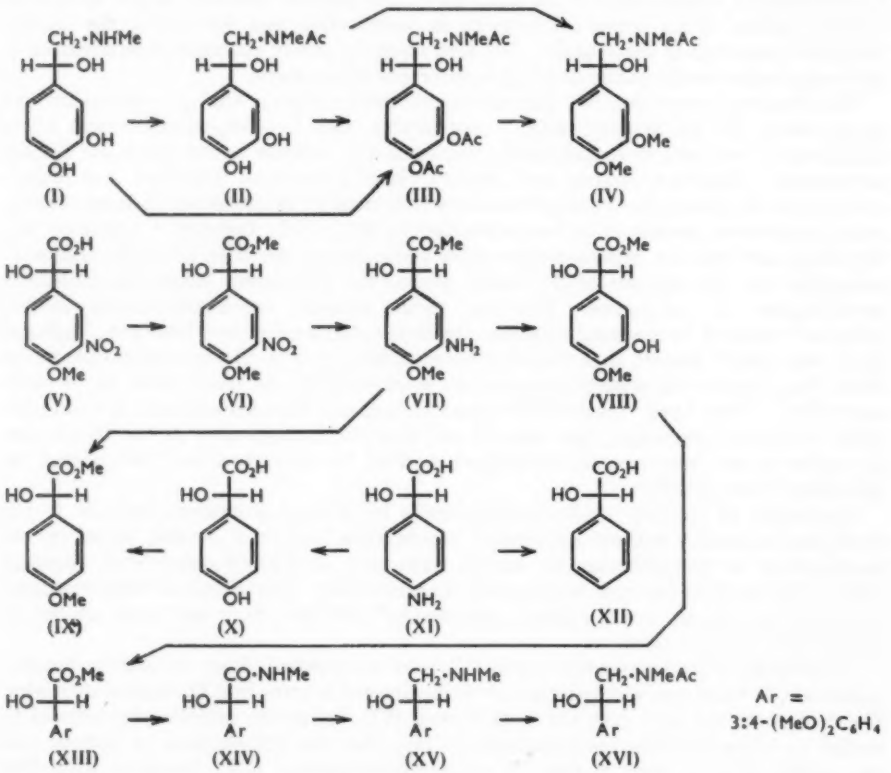
DL-4-Methoxy-3-nitromandelic acid (V) was synthesised from 4-methoxy-3-nitrobenzaldehyde [9] and resolved by means of cinchonine and brucine into the optical antipodes. The dextrorotatory acid gave the methyl ester (VI) which was catalytically reduced to methyl (+)-3-amino-4-methoxymandelate (VII); this was transformed by nitrous acid and copper hydride into methyl (+)-4-methoxymandelate (IX), identical with that

[1] Freudenberg, "Stereochemie," Deuticke, Leipzig, 1932, pp. 697–698.
[2] Blaschko, Holton, and Stanley, *Brit. J. Pharmacol.*, 1948, **3**, 315.
[3] Dalgliesh and Mann, *J.*, 1947, 658.
[4] Dalgliesh, *J.*, 1953, 3323.
[5] Bolhofer, *J. Amer. Chem. Soc.*, 1954, **76**, 1322.
[6] Hartman, Pogrund, Drell, and Clark, *ibid.*, 1955, **77**, 816.
[7] Drell, *ibid.*, p. 5429.
[8] Pratesi and Grassi, *Il Farmaco, Ed. Sci.*, 1953, **8**, 86.
[9] Pratesi, La Manna, Campiglio, and Ghislandi, 16th Internat. Congr. Pure Appl. Chem., Paris, 1957, Abs. Papers, Vol. II, p. 143; *Il Farmaco, Ed. Sci.*, 1957, **12**, 993.

obtained from L(+)-4-hydroxymandelic acid (X) by means of diazomethane. We know that (+)-4-hydroxymandelic acid (X) has the L-configuration because it was obtained [10] from L(+)-4-aminomandelic acid (XI) which Fredga and Andersson [11] converted into L(+)-mandelic acid (XII).

Treating the ester (VII) with nitrous acid and copper sulphate gave methyl L(+)-3-hydroxy-4-methoxymandelate (VIII), which was methylated by diazomethane to oily methyl L(+)-3 : 4-dimethoxymandelate (XIII); when treated with methylamine, this furnished the L(+)-*N*-methylamide (XIV), reduced by lithium aluminium hydride in tetrahydrofuran to oily L(+)-O^3O^4-dimethyladrenaline (XV) (characterised as chloroplatinate).

It was next necessary to prepare this dimethyl ether from an optically active adrenaline. But natural adrenaline was too insoluble for methylation by diazomethane: racemic adrenaline is somewhat more soluble and can be thus methylated, though in very poor yield.[9] L(+)-O^3O^4-Dimethyladrenaline (XV) was therefore acetylated under the conditions



described by Welsh [12] for adrenaline to yield the amide (XVI), m. p. 123—124°, $[\alpha]_D^{18}$ +77·4°. Natural (−)-adrenaline was acetylated by the method used by Bretschneider [13] for the racemic compound, yielding (+)-*N*-acetyladrenaline (II), which with diazomethane gave the optical antipode (IV) of (XVI); this had m. p. 123—124°, $[\alpha]_D^{17}$ −77·4°.

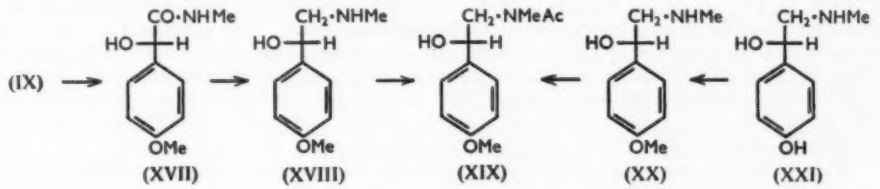
[10] Pratesi, La Manna, and Grassi, *Il Farmaco, Ed. Sci.*, 1955, **10**, 563.
[11] Fredga and Andersson, *Arkiv Kemi, Mineralog. Geol.*, 1941, **14**, *B*, 38.
[12] Welsh, *J. Amer. Chem. Soc.*, 1952, **74**, 4967.
[13] Bretschneider, *Monatsh.*, 1948, **78**, 77.

Under the acetylation conditions described by Welsh,[13] the amide (II) was transformed into (−)-O^3O^4N-triacetyladrenaline (III), identical with that which Welsh obtained by direct acetylation of (−)-adrenaline. With wet diazomethane compound (III) also gave the antipode (IV) of (XVI).

As a result of these transformations, natural lævorotatory adrenaline clearly possesses the configuration (I).

The configuration of the *p*-hydroxyphenyl analogue (" Sympatol," " Synephrine ") was determined similarly, methyl L(+)-4-methoxymandelate (IX) being transformed into L(+)-4-methoxy-*N*-methylmandelamide (XVII), which by reduction with lithium aluminium hydride gave the oily L(+)-O^4-methyl derivative (XVIII). On acetylation this yielded the L(+)-acetamide (XIX), m. p. 119—121°, $[\alpha]_D^{17}$ +93·9°. The same compound, m. p. 119—121°, $[\alpha]_D^{17}$ +91·3°, was obtained from the (+)-amine (XXI) by methylation (⟶ XX) and acetylation. Therefore, the configuration of the lævorotatory drug is the same as that of natural adrenaline (I) [the opposite of (XXI)].

On the basis of the sequence rule,[14] natural lævorotatory adrenaline and its lævorotatory *p*-hydroxyphenyl analogue are (*R*)-forms.



Our work also provides a method of establishing the configuration of the β carbon atom in the 3 : 4-dihydroxyphenylserines, and of the sympathomimetic amines and related compounds in general, some of which have recently become of increased biological interest in connection with central action and the metabolism of adrenaline and noradrenaline.

Experimental

Resolution of DL-*4-Methoxy-3-nitromandelic Acid* (V).—Cinchonine (58·9 g., 0·2 mole) was added to a solution of 4-methoxy-3-nitromandelic acid (45·4 g., 0·2 mole) in boiling 1 : 4 (v/v) aqueous ethanol (560 ml.). The hot solution was treated with charcoal and filtered, and crystals (*A*) (55·3 g.) were collected 24 hr. later. Fraction A had m. p. 166—167°, $[\alpha]_D^{18}$ +156·0° (0·3—0·4% w/v in $CHCl_3$) and gave an acid with $[\alpha]_D^{18}$ +63·4° (0·2—0·3% w/v in EtOH). Four crystallisations from 80% ethanol gave *cinchonine* (+)-*4-methoxy-3-nitromandelate* (29·5 g.) of constant m. p. (190—191°) and rotation {$[\alpha]_D^{18}$ +175·2° (0·3—0·4% w/v in $CHCl_3$)} (Found: C, 62·0; H, 6·4; N, 7·8; H_2O, 3·4. $C_{19}H_{22}ON_2,C_9H_9O_6N,H_2O$ requires C, 62·3; H, 6·2; N, 7·8; H_2O, 3·3%).

This cinchonine salt (12·5 g.), dissolved in 0·1N-sulphuric acid (18 ml.) and extracted with ether, gave the (+)-*acid* (V) (4·9 g.), m. p. 96—97°, $[\alpha]_D^{17}$ +119·0° (0·26% w/v in EtOH) (Found: C, 47·3; H, 4·0; N, 6·1. $C_9H_9O_6N$ requires C, 47·6; H, 4·0; N, 6·2%).

The mother-liquor from fraction *A* was concentrated *in vacuo* below 40° to a syrup (*B*) from which crude (−)-4-methoxy-3-nitromandelic acid (18 g.), $[\alpha]_D^{17}$ −79·5° (0·44% w/v in EtOH), was obtained. This acid (17·45 g.) in boiling 80% ethanol (100 ml.) was treated with brucine (30·2 g.), and the solution cooled, seeded, and left overnight. The *brucine salt* obtained (31·3 g.) had m. p. 95—100°, $[\alpha]_D^{17}$ −58·1° (0·7% w/v in $CHCl_3$); crystallised to constant m. p. and rotation from 80% ethanol, it had m. p. 106—107°, $[\alpha]_D^{17}$ −60·3° (0·7% w/v in $CHCl_3$) (Found: C, 60·0; H, 6·1; N, 6·5; H_2O, 2·7. $C_{23}H_{26}O_4N_2,C_9H_9O_6N,H_2O$ requires C, 60·1; H, 5·8; N, 6·6; H_2O, 2·8%). The (−)-*acid* (V) (2·05 g.), obtained from the brucine salt (6·2 g.), had m. p. 96—97°, $[\alpha]_D^{18}$ −118·5° (0·25% w/v in EtOH) (Found: C, 47·5; H, 4·1; N, 6·3%).

[14] Cahn, Ingold, and Prelog, *Experientia*, 1956, **12**, 81.

Methyl (+)-3-*Amino*-4-*methoxymandelate* (VII).—Pure (+)-4-methoxy-3-nitromandelic acid (50·0 g.) was boiled in methanol (100 ml.) with concentrated sulphuric acid (5 ml.) for 8 hr. The solution was then concentrated *in vacuo* and the crystals (45·5 g.) were collected and washed with saturated aqueous sodium carbonate. Two crystallisations from benzene gave *methyl* (+)-4-*methoxy*-3-*nitromandelate* (VI), m. p. 81—82°, $[\alpha]_D^{17}$ +104·5° (0·42% w/v in EtOH) (Found: C, 49·6; H, 4·7; N, 5·9. $C_{10}H_{11}O_6N$ requires C, 49·8; H, 4·6; N, 5·8%).

The ester (44 g.) in ethanol (230 ml.) was reduced by hydrogen over 5% palladium–alumina at room temperature and 4 kg./cm.^{2}. The catalyst was removed and the solution concentrated *in vacuo* under nitrogen. The *amino-ester* (VII), recrystallised twice from ethanol (yield 30·1 g.), had m. p. 112—113°, $[\alpha]_D^{17}$ +134·3° (0·42% w/v in EtOH) (Found: C, 57·1; H, 6·1; N, 6·6. $C_{10}H_{13}O_4N$ requires C, 56·9; H, 6·2; N, 6·6%).

(+)-3 : 4-*Dimethoxy*-N-*methylmandelamide* (XIV).—Methyl (+)-3-amino-4-methoxymandelate (10·5 g.) was diazotised at −5° in sulphuric acid (27 ml.; 25% v/v) with sodium nitrite (15·4 ml. of 25% solution), and the solution added dropwise to copper sulphate solution (150 g. in 300 ml. of water) at 80—85°. The whole was extracted with ether (8 × 250 ml.), and the extract concentrated, washed with sodium hydrogen carbonate solution and water, dried (Na_2SO_4), and evaporated. *Methyl* (+)-3-*hydroxy*-4-*methoxymandelate* (VIII) (3·7 g.) crystallised from benzene and had m. p. 118—119°, $[\alpha]_D^{17}$ +129·5° (0·56% w/v in EtOH) (Found: C, 56·8; H, 5·9. $C_{10}H_{12}O_5$ requires C, 56·6; H, 5·7%). This ester (1·5 g.) in methanol (45 ml.) was kept for 24 hr. in an ethereal solution of diazomethane (6 g.). The solution was evaporated *in vacuo*, the residue taken up in a little methanol, and excess of anhydrous methylamine added. After 24 hr. at 0° the mixture was concentrated *in vacuo* and the residue stirred with benzene. (+)-3 : 4-*Dimethoxy*-N-*methylmandelamide* (XIV) so obtained crystallised from ethyl acetate; it had m. p. 153—154°, $[\alpha]_D^{20}$ +81·7° (0·9% w/v in $CHCl_3$), $[\alpha]_D^{18}$ +31·5° (0·87% w/v in EtOH) (Found: C, 58·4; H, 6·9; N, 6·5. $C_{11}H_{15}O_4N$ requires C, 58·7; H, 6·7; N, 6·2%).

The carbonate washings from the preparation of methyl (+)-3-hydroxy-4-methoxymandelate gave, on acidification and ten extractions with ether, a dextrorotatory oily acid which on treatment with diazomethane and then methylamine afforded more of the (+)-amide (XIV).

In another run the (+)-amide {m. p. 153—154°, $[\alpha]_D^{20}$ +81·7° (0·93% w/v in $CHCl_3$)} was obtained in 47·4% yield directly from the ester (VII) without isolation of the intermediates (Found: C, 58·6; H, 6·8; N, 6·3%).

(+)-N-*Acetyl*-O^3O^4-*dimethyladrenaline* (XVI).—(+)-3 : 4-Dimethoxy-*N*-methylmandelamide (3 g.) in hot anhydrous tetrahydrofuran (120 ml.) was added dropwise during 15 min. to a stirred suspension of lithium aluminium hydride (1 g.) in tetrahydrofuran at 70—75°. Stirring was continued for 8 hr. at 70—75°. The next day the mixture was treated with a saturated solution of Rochelle salt, then filtered, and the tetrahydrofuran distilled of *in vacuo*. The residual aqueous solution was extracted with chloroform (8 × 100 ml.). The chloroform extracts were washed with a little water, dried (Na_2SO_4), and evaporated *in vacuo*. The residual oily (+)-O^3O^4-dimethyladrenaline (XV) (1·9 g.) did not crystallise, but was characterised as its *chloroplatinate*, m. p. 152—153° (from ethanol) [Found: C, 31·9; H, 4·6; Pt, 23·7. $(C_{11}H_{17}O_3N)_2,H_2PtCl_6$ requires C, 31·7; H, 4·4; Pt, 23·5%].

(+)-O^3O^4-Dimethyladrenaline (0·544 g., 19·3%), obtained as an oil from the chloroplatinate by basification and chloroform-extraction, was suspended in sodium hydrogen carbonate solution (5·4 g. in 20 ml. of water) and treated with acetic anhydride (3·3 ml.). N-*Acetyl*-O^3O^4-*dimethyladrenaline* (XVI) (0·24 g.) was isolated by chloroform-extraction and crystallised from benzene (6 ml.); it had m. p. 123—124°, $[\alpha]_D^{18}$ +77·4° (1·13% w/v in $CHCl_3$) (Found: C, 61·6; H, 7·6; N, 5·6. $C_{13}H_{19}O_4N$ requires C, 61·6; H, 7·6; N, 5·5%).

(+)-N-*Acetyladrenaline* (II).—Natural (−)-adrenaline {22 g.; m. p. 211—212°, $[\alpha]_D^{17}$ −50·6° (0·3 g. in 1·56 ml. of N-HCl +2·44 ml. of H_2O)} was acetylated as described by Bretschneider [12] for (±)-adrenaline. (+)-N-*Acetyladrenaline* (8·5 g.), recrystallised from water, had m. p. 162—163°, $[\alpha]_D^{20}$ +8·5° (2% w/v in H_2O) (Found: C, 58·5; H, 6·9; N, 6·3. $C_{11}H_{15}O_4N$ requires C, 58·7; H, 6·7; N, 6·2%).

(−)-O^3O^4N-Triacetyladrenaline (III), obtained by direct acetylation of (−)-adrenaline by Welsh's method,[12] had m. p. 95—96° (from benzene), $[\alpha]_D^{20}$ −87·4° (1% w/v in $CHCl_3$) (Found: C, 58·4; H, 6·4; N, 4·7. Calc. for $C_{18}H_{19}O_6N$: C, 58·2; H, 6·2; N, 4·5%). It was also obtained when (+)-*N*-acetyladrenaline (2 g.), suspended in aqueous sodium hydrogen carbonate (60 g. in 200 ml. of water), was treated with acetic anhydride (4 × 7·5 ml.): the

triacetyladrenaline (1·6 g.), obtained by chloroform-extraction and recrystallisation from benzene, had m. p. 95—96°, $[\alpha]_D^{17}$ −89·5° (0·96% w/v in $CHCl_3$).

(−)-*N*-*Acetyl*-O^{3}O^4-*dimethyladrenaline* (IV).—(+)-*N*-Acetyladrenaline (3 g.) in methanol (200 ml.) was treated in several portions with a large excess of ethereal diazomethane with cooling and shaking. After 24 hr. the mixture was evaporated *in vacuo*. The solid residue (2·7 g.) was treated with benzene and recrystallised from the same solvent. The product (2·1 g.) had m. p. 123—124°, $[\alpha]_D^{17}$ −77·4° (1% w/v in $CHCl_3$) (Found: C, 61·4; H, 7·7; N, 5·7%).

The same product was obtained by treating (−)-triacetyladrenaline (10 g.) in methanol (70 ml.) with ethereal diazomethane provided a trace of water was present. Recrystallisation from benzene gave the pure product (6·7 g.).

Methyl (+)-4-*Methoxymandelate* (IX).—(*a*) Diazotised methyl (+)-3-amino-4-methoxymandelate (VII) (8·4 g. in 44 ml. of 25% v/v sulphuric acid) was added during 30 min. to a violently agitated suspension of copper hydride, which was prepared as follows: sodium hypophosphite (49·6 g.) in water (96 ml.) and sulphuric acid (132·8 ml.; 25% v/v) was heated to 50—60° and added during 30 min. to a stirred solution of copper sulphate (36·8 g.) in water (72 ml.) and the resulting suspension allowed to cool.

After being stirred for another hour the reaction mixture was extracted with ether (20 × 200 ml.). The combined extracts were concentrated *in vacuo*, then washed with saturated sodium hydrogen carbonate solution and a little water, dried (Na_2SO_4), and evaporated. The solid residue (1·65 g.) was recrystallised thrice from ligroin (b. p. 75—120°) and pure methyl (+)-4-methoxymandelate [15] (1·2 g.) obtained {m. p. 63—64°, $[\alpha]_D^{18}$ +138·0° (3% w/v in EtOH)} (Found: C, 61·2; H, 6·4. Calc. for $C_{10}H_{12}O_4$: C, 61·2; H, 6·2%). The bicarbonate washings on acidification and ether-extraction gave (+)-4-methoxymandelic acid [16] (2·8 g.). Three crystallisations from benzene gave the pure acid, m. p. 105—106°, $[\alpha]_D^{18}$ +141·5° (2·45% w/v in H_2O) (Found: C, 59·1; H, 5·8. Calc. for $C_9H_{10}O_4$: C, 59·3; H, 5·5%).

(*b*) (+)-4-Hydroxymandelic acid was obtained from (±)-4-hydroxymandelic acid [17] by precipitation of its brucine salt in 80% ethanol. After repeated crystallisation of the brucine salt from 80% ethanol, the acid was liberated by sulphuric acid, extracted with ether, and recrystallised from benzene.

Ellinger and Kotake [18] gave, for the anhydrous dextrorotatory acid, m. p. 103—104° and $[\alpha]_D$ +144·4° (1·5% w/v in H_2O). According to Pratesi, La Manna, and Grassi [19] the acid has m. p. 114—115°, $[\alpha]_D^{21}$ +154·7° (1·36% w/v in H_2O). The sample of (+)-acid used by us had m. p. 113—114°, $[\alpha]_D^{18}$ +128·6° (1·2% w/v in H_2O) (Found: C, 57·0; H, 5·0. Calc. for $C_8H_8O_4$: C, 57·1; H, 4·8%).

(+)-4-Hydroxymandelic acid (0·94 g.) in methanol (20 ml.) was treated with an excess of ethereal diazomethane. After 70 hr. at room temperature, the solution was concentrated *in vacuo*. The solid residue was repeatedly crystallised from ligroin (b. p. 75—120°), giving *methyl* (+)-4-*methoxymandelate* (0·41 g., 37·3%), m. p. 63—64°, $[\alpha]_D^{18}$ +136·1° (2·4% w/v in EtOH) (Found: C, 61·1; H, 6·3%).

(+)-4-*Methoxy*-N-*methylmandelamide* (XVII).—This *amide* was prepared from methyl (+)-4-methoxymandelate (5·5 g.) in methanol (50 ml.) by treatment with anhydrous methylamine as described for the 3 : 4-dimethoxymethylamide. The product (5·37 g.), recrystallised from benzene, had m. p. 107—108°, $[\alpha]_D^{18}$ +94·6° (1% w/v in $CHCl_3$) (Found: C, 61·5; H, 6·9; N, 7·3. $C_{10}H_{13}O_3N$ requires C, 61·5; H, 6·7; N, 7·2%).

(+)-N-(2-*Hydroxy*-2-4′-*methoxyphenylethyl*)-N-*methylacetamide* (XIX).—(*a*) (+)-4-Methoxy-*N*-methylmandelamide (XVII) (2 g.) in anhydrous tetrahydrofuran (130 ml.) was reduced by lithium aluminium hydride (0·65 g.) as described above. The product (1·5 g.) was an oil. With acetic anhydride (7·5 ml.) and sodium hydrogen carbonate (12 g.) in water (40 ml.) it gave the (+)-N-*acetyl derivative* (50% crude; 16% pure, from EtOH), m. p. 119—121°, $[\alpha]_D^{17}$ +93·9° (0·69% w/v in $CHCl_3$) (Found: C, 64·4; H, 7·8; N, 6·4. $C_{12}H_{17}O_3N$ requires C, 64·5; H, 7·7; N, 6·3%).

(*b*) (+)-2-Hydroxy-2-4′-hydroxyphenyl-*N*-methylethylamine was obtained by resolution of the racemic compound with ammonium bromocamphorsulphonate. In agreement with Legerlotz [19]

[15] McKenzie and Pirie, *Ber.*, 1936, **69**, 869.
[16] Knorr, *Ber.*, 1904, **37**, 3172.
[17] Ladenburg, Folkers, and Major, *J. Amer. Chem. Soc.*, 1936, **58**, 1294.
[18] Ellinger and Kotake, *Z. physiol. Chem.*, 1910, **65**, 410.
[19] Legerlotz, D.R.-P. 543,529; *Chem. Zentr.*, 1932, I, 2867.

XUM

it had m. p. 179—180°, $[\alpha]_D^{17}$ +61·5° (0·12% w/v in H_2O). A suspension of it (1 g.) in methanol (50 ml.) was kept in ethereal diazomethane at room temperature. After 70 hr. the solution was concentrated *in vacuo*, and the residue taken up in chloroform, washed with aqueous sodium hydroxide, and dried (Na_2SO_4). The (+)-4-methoxy-derivative was obtained as an oil (0·71 g.). It was acetylated as described above, giving the (+)-*N*-acetyl derivative (18·7%), m. p. and mixed m. p. 119—121°, $[\alpha]_D^{17}$ +91·3° (0·73% w/v in $CHCl_3$) (Found: N, 6·4%).

The authors are indebted to Dr. M. T. Cuzzoni for microanalyses and to the Italian "Consiglio Nazionale delle Ricerche" for finance.

Istituto di Chimica Farmaceutica,
Università di Pavia, Italy.

[*Received, December 12th*, 1957.]

427. *Water-soluble Complexes of Niobium (Columbium) and Tantalum. Part II.*[1] *The Dissolution of Niobic and Tantalic Acids in Amine Solutions.*

By Fred Fairbrother, Derek Robinson, and John B. Taylor.

Freshly precipitated niobic acid dissolves in dilute aqueous solutions of aliphatic amines, to form complexes which can be isolated by evaporation or by precipitation with organic solvents. Complexes of niobic acid with eleven amines have been isolated and its solubility in four others has been examined. The complexes vary somewhat in composition but generally contain from about one to three niobium atoms per molecule of amine. The complexes are diffusible through a dialysis membrane, but molecular-weight determinations show that the units are polynuclear.

The dissolution has some of the characteristics of a colloid dispersion and can be reversed by increasing the ionic strength by addition of neutral salts. The dissolution and ageing of the niobic acid are competitive processes and an aged precipitate does not dissolve. Dissolution is largely determined by the basic dissociation constant of the amine.

In spite of the complexing power of many basic nitrogen compounds, no water-soluble complexes of niobium or tantalum with nitrogen compounds appear to have been reported, apart from those with (2-hydroxyethyl)amines described in Part I.[1] Several non-aqueous solutions of amines have, however, been used in solvent-extraction processes [2] in which the niobium or tantalum, usually in the form of an inorganic acid complex, is extracted from an aqueous phase into an organic solution of an amine, though no definite complexes appear to have been isolated from such systems. Also, anhydrous complexes of amines with niobium pentachloride have been described.[3] There is therefore experimental evidence that amines are able to attach themselves as ligands to the niobium atom.

We have now studied the dissolution of niobic and tantalic acid in aqueous solutions of a variety of amines. As in solutions of α-hydroxy-acids, tantalic acid was found in all cases examined to be very much less soluble than niobic acid, by a factor of as much as 10^3 under comparable conditions. The present paper therefore is concerned chiefly with the dissolution of niobic acid, the study of tantalic acid complexes being limited to a few experiments for comparison.

Freshly precipitated and washed niobic acid was found to be more or less easily soluble in dilute solutions of a number of primary, secondary, and tertiary aliphatic amines. From these solutions, by vacuum-evaporation, alone or combined with precipitation by alcohol and ether, solid complexes were obtained. Table 1 lists the amines used and

[1] Part I, Fairbrother and Taylor, *J.*, 1956, 4946.
[2] Leddicotte and Moore, *J. Amer. Chem. Soc.*, 1952, **74**, 1618; Ellenburg, Leddicotte, and Moore, *Analyt. Chem.*, 1954, **26**, 1045; Foos and Wilhelm, U.S.A.E.A. publ. ISC—694, 1954, 20.
[3] Fowles and Pleass, *J.*, 1957, 2078.

XUM

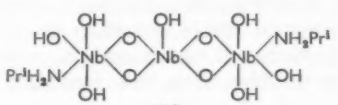
analyses of a number of the products isolated. From this can be seen the variable composition of the complexes, but in almost every case the ratio of atoms of niobium to molecules of amine lies between one and three. Niobic acid was also found to be soluble in aqueous solutions of trimethylamine, ethylamine, di*iso*propylamine, and *cyclo*hexylamine. The products obtained by precipitation with alcohol and ether were white powders: those

TABLE 1.

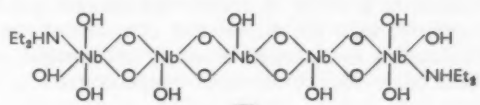
	Found (%)				Found (%)		
Amine	C	Nb_2O_5	Ratio Nb/Amine	Amine	C	Nb_2O_5	Ratio Nb/Amine
NH_2Me	5·6	64·6	1·04	NH_2Pr^i	12·5	65·2	1·41
$NHMe_2$	8·4	59·7	1·28	,,	10·9	66·9	1·66
$NHEt_2$	12·4	71·5	2·08	NH_2Bu	15·1	66·3	1·59
,,	11·6	68·3	2·13	NH_2Bu^i	11·9	71·0	2·16
,,	11·5	68·4	2·15	NH_2Bu^t	11·6	71·3	2·22
,,	17·8	63·6	1·29	Piperidine	18·0	60·5	1·52
NEt_3	13·1	68·3	2·82	,,	17·6	57·4	1·47
NH_2Pr	16·3	56·5	0·94	$(CH_2 \cdot NH_2)_2$	10·3	64·3	1·13

obtained by evaporation usually broke up into small glistening fragments which appeared isotropic under the microscope. In both cases the products gave ill-defined *X*-ray diffraction patterns. It is possible that some structure may exist, since the fracture on drying usually took place along straight lines, often parallel or nearly so.

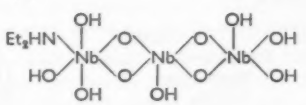
Attempts were made to determine the molecular weights of the complexes cryoscopically in water. The results again showed some variability, probably because of slight hydrolysis during the experiment and because the complex was not composed of a single species. The results however showed unmistakably that the solid species, separated either by vacuum-evaporation or by precipitation with organic solvents, contained aggregrates of from two to five, and exceptionally six, units of niobic acid co-ordinated to one or two molecules of amine. Typical structures suggested therefore are: For *iso*-



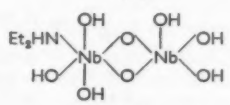
(A)



(B)



(C)



(D)

propylamine (A), which requires C, 12·4%; Nb, 48·1%; *M*, 580. A molecular weight of 600 for such a complex was found experimentally. Singly co-ordinated units may also be present or a mixture of singly and doubly complexed units, *e.g.*, for diethylamine a mixture of (B) (which requires C, 10·7%; Nb, 52·2%; *M*, 891; amine : Nb ratio = 1 : 2·5) with (C) (which requires C, 9·0%; Nb, 52·2%; *M*, 535; amine : Nb ratio = 1 : 3) or (D) (which requires C, 12·21%; Nb, 47·26; *M*, 393; amine : Nb ratio = 1 : 2). A molecular weight of 680 was found for one diethylamine complex.

The size of these units is also consistent with their diffusibility through a dialysis membrane. Migration of the niobium was to the anode. Similarly, electrophoretic experiments showed that the particles in a de-ionised suspension of niobic acid were negatively charged.

The dissolution of niobic acid in an aqueous amine solution has many of the features of a colloid-chemical process in which the amine acts as a peptising agent. Thus, precipitation of niobic acid by ammonia from a solution of the oxalic acid complex, as in the usual method of preparation, yields a product of very variable particle size, dependent

initially mainly upon the temperature of precipitation and the ionic strength of the solution. Immediately after its formation the precipitate starts to age, at a rate which is accelerated by rise of temperature and can be halted for many weeks by storage in a " deep-freeze " cabinet at −30°. This ageing is quite noticeable even overnight at room temperature.

Consequently, the dissolution of niobic acid in an aqueous amine solution depends, not only on the history of the niobic acid, but also on the manner in which the dissolution is carried out, the ageing and dissolution being competitive processes. For example, a given preparation of niobic acid was divided into several portions and these treated in different ways with the same volume of a dilute solution of diethylamine, insufficient in amount to dissolve all the niobic acid. After removal of the excess by centrifugation, the amount in solution was estimated gravimetrically. The results are shown in Table 2.

TABLE 2.

Treatment	g. of Nb_2O_5 in solution	Treatment		g. of Nb_2O_5 in solution
Shaken at room temp. 3½ hr.	0·140	Boiled alone 3½ hr.	shaken with	0·014
,, ,, 48 ,, ...	0·190	Stored at 18° 24 hr. ...	amine for	0·106
Simmered gently 3½ hr.	0·280	Stored at −30° 24 hr.	12 hr.	0·188
Refluxed vigorously 3½ hr.	0·074			

It was found that the most effective method of dissolution was the heating at 70—80° of a preparation of niobic acid which was freshly prepared or had been kept at a low temperature, with a solution of the appropriate amine.

It is a consequence of the heterogeneity of dispersion and the rapid ageing of the precipitate that no two batches of niobic acid are exactly alike and comparative experiments are only possible with different portions, treated, apart from the variable under consideration, in exactly the same manner. Within this limitation it was found that when an excess of niobic acid was shaken for 12 hours with dilute equimolar (0·01M) solutions of a series of amines the amount passing into solution increased, somewhat irregularly, with the dissociation constant of the amine (cf. Table 3). With the more basic amines in sufficient amounts and unaged preparations of niobic acid, dissolution occurs fairly readily at room temperature. In this it differs from the formation of

TABLE 3.

Amine	10^4K	g. of Nb_2O_5 in 100 c.c.	Amine	10^4K	g. of Nb_2O_5 in 100 c.c.
NH_2Bu	4·1	0·201	NH_2Pr^i	5·3	0·494
NH_2Bu^i	2·3	0·295	Piperidine	15·8	0·520
NEt_3	6·4	0·422	$NHEt_2$	12·6	0·617

Niobic acid is insoluble in ammonia ($K = 1·8 \times 10^{-5}$) and in pyridine ($K = 2·3 \times 10^{-9}$) solutions.

complexes with α-hydroxy-acids, undoubtedly as a consequence of the different nature of the two processes. Amine dissolution involves co-ordination of nitrogen to the niobium followed by increased hydration and dispersion of the precipitate, whereas complexing with α-hydroxy-acids involves chelate formation by the elimination of water from two adjacent hydroxyl groups.

The attachment of the amine molecules, to the finer particles at least, appears to take place very rapidly and to be succeeded, as a slower secondary process, by the dispersion of the complex to give a clear solution. Larger particles, though they may take up some amine, are not dispersed even after a long time.

These matters could be followed by observing the change in electrical conductivity (at 25°) on mixing a de-ionised suspension of niobic acid with a solution of an amine. For example, 50 c.c. portions of 1% (v/v) piperidine (~M/10) were mixed separately at 25° with (*a*) 50 c.c. of de-ionised water, (*b*) 50 c.c. of a de-ionised suspension of niobic acid, freshly prepared as described on p. 2078, and containing 0·2008 g. of Nb_2O_5, and (*c*) 50 c.c. of the same suspension which had been heated to 125° ± 5° for 2 hours in an autoclave. The

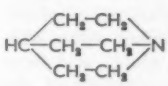
specific conductivity of the de-ionised suspension was negligible compared with those of the mixtures, which were as follows: (*a*) $1{\cdot}80 \times 10^{-3}$ mho; (*b*) at 15 min. after mixing 1·66 mho, but within 4 hr. $1{\cdot}63 \times 10^{-3}$ mho, and in 3 days, by which time the solution had become quite clear, $1{\cdot}58 \times 10^{-3}$ mho where it remained for a further two days. If it is assumed that the complex is relatively non-conducting, the last figure indicates a consumption of amine corresponding to an amine : niobium ratio of about 1 : 1·2, which is within the range of compositions of many of the solid amine complexes. Of the total amount of amine taken up however, nearly two-thirds was taken up in the first few minutes, without any obvious clearing of the solution. This could be due in part to an unobserved dissolution of the finer particles or more probably to co-ordination of amine molecules on the periphery of most of the particles, followed by their slower break up and dispersion.

In contrast, the immediate fall in conductivity of the aged mixture (*c*) was much less, to $1{\cdot}75 \times 10^{-3}$ mho, and only to $1{\cdot}71 \times 10^{-3}$ mho after one week. This corresponds to an absorption of amine about 40% of that by the unaged sample. Longer heating would undoubtedly have decreased the absorption still further. The aged mixture did not become clear even when kept for many weeks.

It is well known that, in many cases, aliphatic monoamines co-ordinate less readily than does ammonia, that secondary amines do so even less, and that, with a number of metal ions, teritary amines have little tendency to co-ordinate at all. On the other hand, it is known that the stability of the ferric ammines, with which perhaps the present series has more in common, is in the reverse direction.[4] As already mentioned, the dissolution of niobic acid in aqueous amine solutions of equimolar concentration appears to depend partly on the basic dissociation constant of the amine. There can be no question however of the dissolution's being due to an increase in the charge : size ratio of the particles due to de-protonation by the base. Both the acid dissociation of the niobic acid (as shown by the low conductivity of a purified suspension) and the proton affinity of the bases are much too small. It is only at very high hydroxyl-ion concentrations, in solutions of strong alkalis, that de-protonation occurs, with the resulting break up of the niobic acid into anions that can subsequently crystallise as alkaline niobates. Even here, as shown by Hauser and Lewite,[5] the process can be reversed, and practically the whole of the alkali removed by dialysis. Also, with a given amine and excess of niobic acid, the amount passing into solution decreases with increasing concentration of amine and the complexes are insoluble in pure amine. In fact, with many amines a convenient alternative to concentration of the solution or precipitation with alcohol and ether was to precipitate the complexes by addition of excess of amine. Thus, a sample of freshly precipitated and washed niobic acid was divided into several equal parts each of which was made up to 100 c.c. with a different volume of amine. The mixtures were shaken for 12 hours in a water-thermostat at 70° and the niobic acid passing into solution estimated. The results were:

Amine solution (% v/v)	2·5	5·0	7·5	10·0	15·0	20·0	60·0
Mg. of Nb_2O_5 dissolved per c.c. of amine ...	237	144	142	84	65	34	5

Bailar [4] has suggested that the instability of tertiary amine complexes of many metal ions may be due to steric factors. A consideration of space models of the various amines used in the present work and the irregular dependence of the dissolution on the basic dissociation constants also suggested that steric factors might play a part. The rôle of steric factors in determining the stabilities of amine addition compounds of trimethylboron has been discussed by Brown,[6] who found that the addition compound of quinuclidine (I) with trimethylboron was much more stable than that between its "open" analogue triethylamine and trimethylboron. Through the kindness of Professor Brown in



(I)

[4] Sidgwick, *J.*, 1941, 433; Bailar, "The Chemistry of the Co-ordination Compounds," Reinhold, New York, 1956, p. 62.
[5] Hauser and Lewite, *Z. angew. Chem.*, 1912, **25**, 100.
[6] Brown, *J.*, 1956, 1248.

supplying a sample of quinuclidine hydrochloride we were able to carry out a similar experiment with niobic acid.

0·2959 g. of quinuclidine hydrochloride was distilled with sodium hydroxide to give 0·002 mole of quinuclidine. A freshly prepared sample of niobic acid was divided into two parts which were shaken, for 12 hours at room temperature, respectively with 100 c.c. of 0·02M-triethylamine and of 0·02M-quinuclidine. After removal of excess of niobic acid by centrifugation, the Nb_2O_5 in solution was found to be, for triethylamine 0·030 g. and for quinuclidine 0·050 g. Since triethylamine and quinuclidine have almost the same basic dissociation constant,[7] it must be concluded that also in the case of the dissolution of niobic acid steric considerations play a part.

A number of experiments were carried out with samples of niobic and tantalic acid prepared under similar conditions in order to compare their reactivitites with given amines. In some cases, for example, in diethylamine, a " solubility " ratio approaching 1000 : 1 in favour of niobium was found. When the two acids were individually precipitated and then mixed, good separation could be achieved by using this difference in solubility in amines. On the other hand, when the niobic and tantalic acids were co-precipitated from the mixed solutions of a complex or prepared from mixed oxides, the dissolved niobium always contained considerable amounts of tantalum. This is clearly a consequence of the polynuclear character of the amine complexes and of the replacement of niobium by tantalum in the oxygen-bridged groups.

Experimental

Niobic and tantalic acid were precipitated by ammonia from a solution in oxalic acid of a melt with pyrosulphate. The cooled fused mass was dissolved in 4% oxalic acid instead of the more concentrated solutions used in Part I. This avoided much of the difficulty with crystallisation of ammonium oxalate from the neutralised solutions and the consequent necessity of keeping the solutions hot during the initial stages of purification. In turn this led to a more active product. The precipitates were washed on the centrifuge, three times with 2% ammonium chloride solution and twice with distilled water. As the washing with water proceeded, the niobic acid showed a tendency to become dispersed. " De-ionised " suspensions were prepared by passing a well-washed reactive suspension four times through a column of Amberlite Monobed Resin (MB3). This effectively removed soluble ions whilst very little niobic acid adhered to the resin: most of this could be removed by distilled water. Such a de-ionised suspension remained stable for many days.

The amines used were purified by fractionation, and solutions of the complexes generally prepared by warming a suspension of about 0·5 g. of Nb_2O_5 in 150 c.c. of 10% v/v amine solution. Complete dissolution required 10—30 min. The volume of solution was then reduced, by evaporation in a vacuum at $\gtrsim 40°$, to a syrup, which was either allowed to dry over silica gel in a vacuum-desiccator or precipitated with alcohol and ether or excess of parent amine. Precipitation with excess of amine, followed by washing with acetone and ether, was especially valuable for the isolation of complexes with the less volatile amines, such as ethylenediamine, where the excess of amine was difficult to remove by evaporation without decomposition of some of the complex.

The complexes were all insoluble in common organic solvents and in the parent amine, but very soluble in water to give solutions with a faint alkaline reaction. In most cases hydrolysis was slow and solutions could be boiled without decomposition. The triethylamine, ethylenediamine, and *cyclo*hexylamine complexes, however, were decomposed in boiling water with precipitation of niobic acid. 3N-Mineral acids and acetic acid precipitated niobic acid from aqueous solutions of the complexes. A quantitative measurement of the stability of the niobic acid–*iso*propylamine complex as a function of pH on addition of dilute hydrochloric acid or sodium hydroxide, indicated a fairly sharply defined region of stability between pH 2·2 and 11·9; outside these limits niobic acid was rapidly precipitated.

The formation and decomposition of the *iso*propylamine complex was found to be particularly

[7] Pearson, *J. Amer. Chem. Soc.*, 1954, **76**, 258.

useful as an analytical tool in another work. Niobium halides or oxyhalides dissolved immediately in 5—10% *iso*propylamine solution with complete hydrolysis without loss. Addition of 3N-acetic acid precipitated niobic acid from the solution in an easily filterable form.

When the solutions of the complexes were warmed with 3N-sodium hydroxide, the niobate was formed and deposited as crystals on cooling.

THE UNIVERSITY, MANCHESTER, 13. [*Received, January 15th*, 1958.]

---

428. 5-*Methoxy*-N-*methyltryptamine*: *A New Indole Alkaloid from* Phalaris arundinacea *L.*

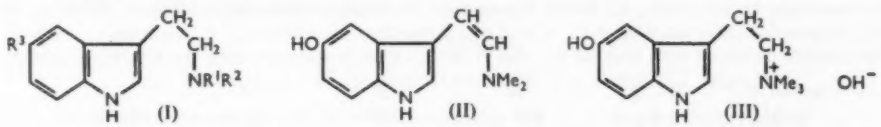
By S. WILKINSON.

5-Methoxy-*N*-methyltryptamine and hordenine (*p*-hydroxyphenethyldimethylamine) have been isolated from reed canary grass (*Phalaris arundinacea* L.).

A REPORT [1] of the occurrence of " staggers " in sheep confined to pastures in which the perennial grass *Phalaris tuberosa* predominates led us to investigate the chemical constituents of a species of *Phalaris* (*P. arundinacea* L.) growing in the grounds of these laboratories.

From this grass, which is free from any fungal parasite, 5-methoxy-*N*-methyltryptamine and hordenine were isolated.

Whilst hordenine has been found in the seedlings of cereals [2] and in the Cactaceae, *Anhalonium* and *Trichocereus*,[2] 5-methoxy-*N*-methyltryptamine is apparently a new naturally-occurring alkaloid and is of interest biogenetically and pharmacologically because of its relation to 5-hydroxytryptamine.



Of the series of tryptamines (I; R^1 = H or Me, R^2 = H or Me; R^3 = H or OH or OMe), all, with the exception of the two 5-methoxytryptamines (I; $R^1 = R^2$ = H, R^3 = OMe) and (I; $R^1 = R^2$ = Me, R^3 = OMe), occur naturally,[3,4] as do dehydrobufotenine (II) and bufotenidine (III).[4]

The total alkaloids from *P. arundinacea* gave, with *p*-dimethylaminobenzaldehyde in 65% v/v sulphuric acid, a green solution which became blue on dilution with water (cf. tryptamine) and with the same reagent in ethanol containing hydrochloric acid, a deep blue, in contrast to gramine and tryptamine which gave pale pink and purple colours, respectively.

Paper chromatography of the alkaloids (Whatman No. 1 paper) with butan-1-ol–water–acetic acid (12 : 5 : 3), followed by spraying with *p*-dimethylaminobenzaldehyde in *cyclo*hexane and treatment with hydrogen chloride, showed the presence of two indoles, a large blue spot (R_f = 0·58) and a smaller pink spot (R_f = 0·70).

[1] 8th Annual Report of the Commonwealth Scientific and Industrial Research Organisation, 1956.
[2] Manske and Holmes, " The Alkaloids," New York, 1949, III, p. 320.
[3] White, *New Zealand Sci. Technol.*, 1944, **25**, *B*, 137; Yarashevski, *J. Gen. Chem.* (*U.S.S.R.*), 1939, **9**, 595; 1940, **10**, 3781; 1941, **11**, 157; Hochstein and Paradies, *J. Amer. Chem. Soc.*, 1957, **79**, 5735; Erspamer, *Rend. Sci. Farm.*, **1**, 1954; Jaques and Schachter, *Brit. J. Pharmacol.*, 1954, **9**, 53; Adams and Weiss, *Nature*, 1956, **178**, 421; Bowden, Brown, and Batty, *ibid.*, 1954, **174**, 925; Collier and Chesher, *Brit. J. Pharmacol.*, 1956, **11**, 186; Mathias, Ross, and Schachter, *Nature*, 1957, **180**, 658.
[4] Wieland, Kons, and Mittasch, *Annalen*, 1934, **513**, 1; Jensen and Chen, *J. Biol. Chem.*, 1936, **116**, 87; Erspamer, *Pharmacol. Rev.*, 1954, **6**, 427.

XUM

The alkaloids were separated by chromatography on alumina, the course of the separation being followed by paper chromatography and colour reactions. The first runnings contained no indoles but from them hordenine was isolated. The later fractions, yielded a crystalline hydrochloride, $C_{12}H_{15}ON,HCl$ ($R_f = 0{\cdot}58$ in the above solvent mixture), containing no phenolic hydroxyl groups and giving a blue colour with sodium nitroprusside and acetone but not with acetaldehyde, characteristic of a secondary amine,[5] hence suggesting the structure methoxy-*N*-methyltryptamine. Comparison of the ultraviolet spectrum with that of tetrahydro-6-methoxycarbazole [6] indicated that the methoxy-group was probably located in the 5-position. Conclusive proof was finally obtained by synthesis of 5-methoxy-*N*-methyltryptamine, the melting points of the hydrochlorides and the ultraviolet spectra [natural hydrochloride in ethanol: $\lambda_{max.}$ 275·6 and 309 mμ ($\varepsilon_{mol.}$ 6470 and 3790); synthetic hydrochloride in ethanol: $\lambda_{max.}$ 275 and 309 mμ ($\varepsilon_{mol.}$ 6470 and 3790)] being identical.

The second, minor, indole alkaloid (R_f 0·70) has not been identified; although concentrating in the mother liquors from which 5-methoxy-*N*-methyltryptamine is crystallised, it is present only in small amounts. It is not gramine but on the paper chromatogram it gives the same colour reaction and has the same R_f as 3-diethylaminomethylindole.

Experimental

Extraction.—Minced grass (4·5 kg.) was extracted at 60° for 5 hr. with ethanol (45 l.). After being kept overnight, the liquor was removed by decanting and pressing, and concentrated under reduced pressure to 2 l.; water (2 l.) was added, and the mixture was heated at 60° for 5 min. and filtered. The pale brown filtrate was saturated with sodium chloride, strongly basified with 20% aqueous sodium hydroxide, and extracted with chloroform (2 × 1·5 l.). The combined chloroform extracts were dried (Na_2SO_4) and concentrated under reduced pressure.

The residue was dissolved in chloroform (10 ml.) and chromatographed on alumina (4 × 20 cm.); elution was continued with chloroform and 5-ml. fractions were collected. Each fraction was tested with: *A*, Millon's reagent; *B*, dimethylaminobenzaldehyde (0·125 g. in 65% sulphuric acid containing 0·1% v/v of 5% ferric chloride solution); *C*, addition of water to the mixture obtained with reagent *B*; and *D*, ferric chloride solution, with the following results:

Fraction no.	Wt. (g.)	*A*	*B*	*C*	*D*
4—11	1	red	brown	green	blue-green
12—60	1·2	brown	green	blue	—

Fractions 4—11 were combined and concentrated under reduced pressure, the residue was dissolved in dry ether, and dry hydrogen chloride was passed through the solution. The precipitated hydrochloride was washed with ether and crystallised from alcohol–acetone giving platelets, m. p. 176—177° (hordenine hydrochloride,[7] m. p. 176·5—177·5°) (Found: C, 59·8; H, 7·7; N, 7·05. Calc. for $C_{10}H_{14}ONCl$: C, 59·6; H, 7·9; N, 6·95%) from which the base was obtained as prisms, m. p. 116—117° (hordenine,[7] m. p. 117—118°), from aqueous alcohol (Found: C, 72·6; H, 8·9; N, 8·7; O, 9·7. Calc. for $C_{10}H_{13}ON$: C, 72·8; H, 9·1; N, 8·5; O, 9·7%). It gave a methiodide, m. p. 228—229° (prisms from ethanol) (hordenine methiodide,[7] m. p. 229—230°) (Found: C, 42·0; H, 5·9; N, 4·6; I, 41·2. Calc. for $C_{11}H_{16}ONI$: C, 43·0; H, 5·9; N, 4·6; I, 41·4%).

Fractions 12—60 were combined and concentrated under reduced pressure and the residue was converted in ether into the hydrochloride, which formed prisms (from ethanol–acetone), m. p. 165—166° (m. p. not depressed on admixture with synthetic 5-methoxy-*N*-methyltryptamine hydrochloride) (Found: C, 60·2; H, 6·8; N, 11·8. Calc. for $C_{12}H_{17}ON_2Cl$: C, 59·9; H, 7·1; N, 11·6%). The *picrate* formed orange-red prisms, m. p. 220—221°, (decomp.) [Found: C, 50·0; H, 4·2; N, 16·0; O, 29·2%; *M* (spectrophotometrically), 431. $C_{12}H_{16}ON_2,C_6H_3O_7N_3$ requires C, 49·9; H, 4·4; N, 16·2; O, 29·6%; *M*, 433).

5-Methoxy-N-toluene-p-sulphonyltryptamine.—5-Methoxytryptamine [8] (6 g.) in benzene

[5] Kharichkov, *J. Russ. Phys. Chem. Soc.*, 1906, **38**, 1407.
[6] Chalmers, Openshaw, and Smith, *J.*, 1957, 1115.
[7] Henry, "The Plant Alkaloids," 4th Edn., Churchill, London, 1949.
[8] Abramovitch and Shapiro, *J.*, 1956, 4589.

(72 ml.) was shaken for 1 hr. with toluene-*p*-sulphonyl chloride (7·2 g.), potassium hydroxide (3·72 g.), and water (36 ml.). After acidification of the solution with hydrochloric acid, the solid was filtered off, washed with water, dried (P_2O_5), and crystallised from benzene, giving plates, m. p. 123—124° (8·9 g.) (Found: C, 62·9; H, 5·8; N, 8·1; S, 9·5. $C_{18}H_{20}O_3N_2S$ requires C, 62·8; H, 5·9; N, 8·2; S, 9·3%).

*5-Methoxy-N-methyl-N-toluene-*p*-sulphonyltryptamine.*—Interaction of 5-methoxy-*N*-toluene-*p*-sulphonyltryptamine (6 g.), ethanol (10 ml.), 80% aqueous sodium hydroxide (3·6 g.), and methyl iodide (3·4 g.) during 12 hr. at room temperature gave prisms (5·5 g.) (from ethanol), m. p. 118—119° (Found: C, 63·7; H, 7·8; S, 8·7. $C_{19}H_{22}O_3N_2S$ requires C, 63·7; H, 7·9; S, 8·95%).

5-Methoxy-N-methyltryptamine.—The toluene-*p*-sulphonyl derivative (5 g.) was dissolved in liquid ammonia (200 ml.) and pellets of sodium were added until the liquid remained blue for some ten min. The colour was discharged by addition of ammonium chloride, the ammonia was evaporated, and the residue dissolved in water (10 ml.). The solution was basified with sodium hydroxide solution and extracted with ether. The ether solution was dried (Na_2SO_4) and the residue distilled (150°/0·05 mm.; bath temp.) to give a pale yellow oil (3 g.). Dry hydrogen chloride was passed through its ethereal solution and the precipitate was washed with ether and crystallised from ethanol–acetone, giving prisms, m. p. 166—167° (Found: C, 60·0; H, 7·0; N, 11·5; O, 7·1; Cl, 14·7. $C_{12}H_{17}ON_2Cl$ requires C, 60·0; H, 7·1; N, 11·7; O, 6·7; Cl, 14·8%).

Thanks are expressed to Dr. H. T. Openshaw for his interest in the work, Dr. A. J. Everett for the spectroscopic determinations, Mr. P. R. W. Baker for the micro-analytical results, Mr. J. F. Spilsbury and Mr. J. P. Evanson for identifying and collecting the samples of grass, and Mr. L. A. Lowe and Mr. D. J. Royall for technical assistance.

WELLCOME RESEARCH LABORATORIES, BECKENHAM, KENT. [*Received, December 19th*, 1957.]

---

429. *The Synthesis of Derivatives of* 1 : 4-*Diphenyldiethylenediphosphine.*

By CHRISTOPHER H. S. HITCHCOCK and FREDERICK G. MANN.

Two syntheses of the diethobromide of 1 : 4-diphenyldiethylenediphosphine are described. This dibromide, when heated under a variety of conditions, underwent rupture of the ring system with the formation of *s*-ethylenebis(ethylphenylphosphine), and the parent 1 : 4-diphenyldiethylenediphosphine could not be thus obtained. Other attempts to prepare the cyclic ditertiary phosphine without a thermal decomposition stage have been investigated without success.

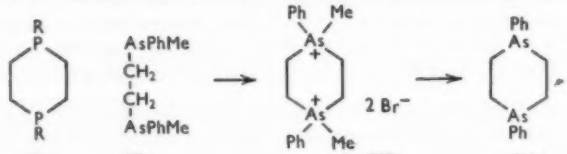
WE have investigated many routes which could possibly lead to the isolation of 1 : 4-disubstituted diethylenediphosphines (systematically 1 : 4-disubstituted 1 : 4-diphospha-*cyclo*hexanes) of type (I). Comparable arsenic compounds were prepared by Jones and Mann,[1] who condensed *s*-ethylenebis(methylphenylarsine) (II) with ethylene dibromide to give 1 : 4-dimethyl-1 : 4-diphenyldiethylenediarsonium dibromide (III) in 21% yield and considerable amorphous material presumably formed by extensive linear condensation: heating the dibromide (III) then gave the diarsine (IV) in 29% yield.

In view of these results, we have converted phenylphosphine (V), by the action of sodium in liquid ammonia, into phenylmonosodiophosphine, which readily reacted with ethyl bromide to form ethylphenylphosphine (VI), a method precisely parallel to that by which Mann and Smith prepared a series of alkylphenylarsines.[2] The phosphine (VI) was then converted *in situ* into the sodio-derivative, which reacted with ethylene dibromide to form *s*-ethylenebis(ethylphenylphosphine) (VII) in 35% overall

[1] Emrys R. H. Jones and Mann, *J.*, 1955, 401.
[2] Mann and Smith, *J.*, 1952, 4544.

XUM

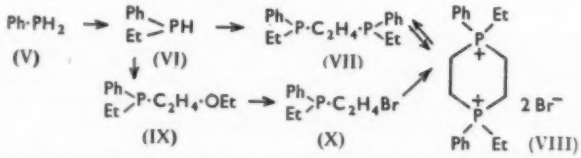
yield from the phosphine (I). It is noteworthy that these groups cannot be introduced in the reverse order into the phosphine molecule. Phenylmonosodiophosphine in ammonia, when treated in turn with one equivalent of ethylene dibromide, sodium, and ethyl bromide, did not furnish the diphosphine (VII), and our experience indicates that ethylene dibromide possibly reacts only with the sodio-derivatives of secondary phosphines.



(I) (II) (III) (IV)

The diphosphine (VII) when heated with ethylene dibromide gave 1 : 4-diethyl-1 : 4-diphenyldiethylenediphosphonium dibromide (VIII), but only in moderate yield.

In an alternative and more efficient synthesis, ethylphenylphosphine (VI) was converted in liquid ammonia into the monosodio-derivative, which with 2-ethoxyethyl iodide formed 2-ethoxyethyl-ethylphenylphosphine (IX) in 63% yield. Hydrogen



bromide converted this phosphine in boiling acetic acid into the liquid 2-bromoethyl-ethylphenylphosphine (X), which underwent self-quaternisation, spontaneously at room temperature and readily in boiling toluene, to form the diphosphonium dibromide (VIII).

The dibromide (VIII) and the corresponding dichloride and dipicrate are highly crystalline and, like the diarsonium dibromide (III), showed no sign of *cis–trans*-isomerism: the two series thus differ from similar piperazine diquaternary salts, which Hanby and Rydon [3] have obtained as geometric isomers.

The thermal decomposition of the dibromide (VIII) was investigated, in the hope that it would entail loss of ethylene and hydrogen bromide, and the formation of 1 : 4-diphenyldiethylenediphosphine (I; R = Ph). In spite of a wide variety of conditions employed, however, this decomposition always caused rupture of the cyclic system, with regeneration of the ethylenebis(ethylphenylphosphine) (VII).

It appears highly improbable, therefore, that 1 : 4-disubstituted diethylenediphosphines (I) can be thus prepared from their diphosphonium dihalides. The thermal decomposition of phosphonium bromides fails signally also for the preparation of various intermediate compounds. For example, 2-bromoethyltriethylphosphonium bromide (XI) on being heated underwent general charring, and the formation of a tertiary phosphine could not be detected: 2-ethoxyethyltriethylphosphonium bromide (XII; R = Et) and

$[Et_3P{\cdot}C_2H_4Br]Br$ (XI) $[REt_2P{\cdot}C_2H_4{\cdot}OEt]Br$ (XII) $[REt_2P{\cdot}C_2H_4{\cdot}PEt_2R]Br_2$ (XIII)

its phenyl analogue (XII; R = Ph) gave similar unsatisfactory results. *s*-Ethylenebis-(triethylphosphonium) dibromide (XIII; R = Et) and the phenyl analogue (XIII; R = Ph) underwent smooth thermal decomposition with the formation of triethyl- and diethyl-phenyl-phosphine respectively, but ditertiary phosphines of type (VII) cannot apparently be prepared in this way. The trimethylene homologue of (XIII; R = Et) also similarly gave triethylphosphine.

To avoid thermal decompositions, therefore, phenylphosphine in liquid ammonia was

[3] Hanby and Rydon, *J.*, 1945, 833.

treated in turn with one equivalent of sodium and of 2-ethoxyethyl iodide, and the process then repeated, to form the liquid di-(2-ethoxyethyl)phenylphosphine (XIV; R = OEt). This phosphine, treated in boiling acetic acid with hydrogen bromide, gave ultimately a viscous syrup, presumably the 2-bromoethyl derivative (XIV; R = Br); it was treated

$Ph{\cdot}P(C_2H_4R)_2$ (XIV) $PH_2(C_2H_4{\cdot}OH)$ (XV) $PH(C_2H_4{\cdot}OH)_2$ (XVI) $P(C_2H_4{\cdot}OH)_3$ (XVII)

without delay with phenylphosphinebis(magnesium bromide), $Ph{\cdot}P(MgBr)_2$, in the hope of obtaining the 1 : 4-diphenyl compound (I; R = Ph), but no decisive product could be isolated. This result is in marked contrast to the ready reaction of di-(2-bromoethyl)-aniline with this reagent [4] and with the arsenic analogue, $Ph{\cdot}As(MgBr)_2$,[5] to form the highly crystalline hexahydro-1 : 4-diphenyl-1 : 4-azaphosphine and -azarsine respectively. The present failure may have been due to impurities in the phosphine (XIV; R = Br).

It has been claimed [6] that phosphine reacts with ethylene oxide to give the 2-hydroxyethylphosphines (XV), (XVI), and (XVII) in low yield, but we find that phenylphosphine, when heated with ethylene oxide in sealed tubes, formed solely polymeric material: the desired di-(2-hydroxyethyl)phenylphosphine (XIV; R = OH), moreover, could not be obtained by the action of ethylene oxide on the magnesium derivative, $Ph{\cdot}P(MgBr)_2$.

Phenylphosphine in the presence of potassium carbonate underwent no reaction when heated in nitrogen under reflux with ethylene dibromide, bromohydrin, or chlorohydrin.

Other methods for the preparation of cyclic ditertiary diphosphines of type (I) are now being investigated.

It is noteworthy that the basic strength of triethylphosphine enables it to form a picrate which can be recrystallised unchanged from hot ethanol: this is apparently the first recorded example of a tertiary phosphine picrate having a stability of this order.

The therapeutic properties of the diphosphonium dichloride (as VIII) have been investigated by Imperial Chemical Industries Limited, Pharmaceuticals Division, who find that it is ineffective against a *Trypanosoma congolense* infection in mice and against *Streptococcus haemolyticus in vitro*. It showed feeble activity against a mouse nematode infection, but much less than that exhibited by some of the phosphoric esters in current use.

Experimental

Compounds were colourless unless otherwise stated.

Reactions in Liquid Ammonia.—The following general directions apply to all such experiments recorded below. Phenylphosphine (V) (5—40 g.) was pipetted directly from an ampoule into liquid ammonia (25—250 c.c.) in a flask through which nitrogen was passing, immersed in acetone–solid carbon dioxide. Ether (5—40 c.c.), used to wash the ampoule, was added. Small pieces of sodium (1 equiv.) were dropped into the stirred solution, each piece dissolving exothermically forming a local characteristic blue colour which was rapidly replaced by the orange colour of the sodiophosphine. When a permanent blue-black colour indicated a slight excess of sodium, the solution was stirred for 15 min., and the first alkyl halide (1 mol.) in ether (3—20 c.c.) added during 10 min., giving first the orange colour and ultimately an almost colourless suspension of a white precipitate. Sodium (*ca.* 1 equiv.) was added as before (the reaction being now slower) until the blue-black coloration became permanent, and the mixture was then stirred for at least 1 hr. The second alkyl halide (*ca.* 1 mol.) in ether (3—20 c.c.) was added dropwise until the orange colour faded to white. The bath was removed, ether added, and the ammonia allowed to boil away. Cold boiled water (20—100 c.c.) was cautiously added, and the ethereal phosphine solution separated under nitrogen, dried, and distilled.

s-*Ethylenebis(ethylphenylphosphine)* (VII).—This was prepared from phenylphosphine (V) (24·8 g.) in liquid ammonia (250 c.c.), sodium (5·2 g., 1 equiv.), ethyl bromide (24·6 g., 1 mol.), sodium as before, and ethylene dibromide (21·1 g., 0·5 mol.). Distillation gave the fractions: (*a*) b. p. 55—60°/0·4 mm., 9·0 g., probably diethylphenylphosphine, (*b*) b. p. 148—165°/0·4 mm.,

[4] Mann and Millar, *J.*, 1952, 3039.
[5] Beeby and Mann, *J.*, 1951, 886.
[6] Knunyants and Sterlin, *Compt. rend. Acad. Sci. U.R.S.S.*, 1947, **56**, 49; *Chem. Abs.*, 1948, **42**, 519.

XUM

12·2 g. (36%), the *diphosphine* (VII), which solidified, and had m. p. 69—70° after crystallisation from ethanol (Found: C, 71·4; H, 8·1. $C_{16}H_{24}P_2$ requires C, 71·5; H, 8·0%). An ethereal solution of the diphosphine, when treated with methyl iodide, deposited the crystalline *dimethiodide*, m. p. 199—200° (from methanol) (Found: C, 41·1; H, 5·3. $C_{20}H_{30}I_2P_2$ requires C, 41·0; H, 5·2%). A boiling ethanolic solution, treated with ethyl bromide, gave the *diethobromide*, m. p. 255—257° (from ethanol) (Found: C, 50·6; H, 6·9. $C_{22}H_{34}Br_2P_2$ requires C, 50·8; H, 6·6%).

The m. p. of the pure diphosphine was unaffected when the crystals were exposed to the air at room temperature for 24 hr.

When in a similar experiment to the above the order of addition of the ethyl bromide and ethylene dibromide was reversed, distillation gave diethylphenylphosphine, b. p. 200—218° (61% calc. on the ethyl bromide), identified as triethylphenylphosphonium bromide, m. p. 184—186° (lit.,[7] 187—188°) (Found: C, 52·6; H, 7·4. Calc. for $C_{12}H_{20}BrP$: C, 52·4; H, 7·3%), and as-*dibromobis(diethylphenylphosphine)palladium*, orange crystals, m. p. 132—133° (from ethanol) (Found: C, 40·2; H, 5·1. $C_{20}H_{30}Br_2P_2Pd$ requires C, 40·1; H, 5·1%).

In another experiment, phenylphosphine in liquid ammonia was treated with sodium (1 equiv.) and ethylene dibromide (0·5 mol.), and the addition of these reagents then repeated. The resulting crude yellow viscous product did not crystallise or give any crystalline derivative, and almost certainly was not the diphosphine (I; R = Ph).

1 : 4-*Diethyl*-1 : 4-*diphenyldiethylenediphosphonium Dibromide* (VIII).—A solution of the diphosphine (VII) (0·5 g.) and ethylene dibromide (0·6 g., 2 mols.) in ethanol (10 c.c.) was boiled under reflux in nitrogen for 2 hr., and evaporated. The gummy residue, when washed with ether and recrystallised from ethanol, gave the *dibromide* (VIII), which decomposed at *ca.* 370° without melting (Found: C, 48·9; H, 5·7%; *M*, apparent, cryoscopic in 0·57% aqueous solution, 165, in 1·1% solution, 167. $C_{26}H_{32}Br_2P_2$ requires C, 49·0; H, 5·8%; *M*, 490). The total ionisation of a uni-bivalent salt, indicated by the molecular-weight determinations, was confirmed by the molecular conductivity, Λ_M, 215 mho/cm.^{2}, of an aqueous solution, dilution 1480 l., at 20°.

It is noteworthy that when a mixture of the diphosphine (VII) and ethylene dibromide (1 or 5 mols.) in methanol or ethanol was heated in nitrogen either under reflux or in a sealed tube at 100°, the final gummy residue could not be obtained crystalline: only the above use of the dibromide (2 mols.) proved successful.

The dibromide (VIII) in aqueous solution gave a yellow *dipicrate*, m. p. 240—245° (decomp.) after crystallisation from much water (Found: C, 48·7; H, 4·3; N, 10·9. $C_{32}H_{32}O_{14}N_6P_2$ requires C, 48·9; H, 4·1; N, 10·7%). The aqueous solution of the dibromide, when shaken with an excess of silver chloride for 10 hr., filtered, and evaporated, gave the *dichloride*, which, after recrystallisation from ethanol and drying at 100°/0·1 mm., decomposed at *ca.* 350° without melting (Found: C, 59·8; H, 7·2. $C_{26}H_{32}Cl_2P_2$ requires C, 59·8; H, 7·0%).

The diphosphine (VII) did not react with ethylene dichloride: it reacted readily with trimethylene or *o*-xylylene dibromide, but in each case the viscous syrupy product could not be purified or converted into a satisfactory derivative.

2-*Ethoxyethyl-ethylphenylphosphine* (IX).—Phenylphosphine (V) (22·5 g.) in ammonia (150 c.c.), when treated with sodium (4·7 g., 1 equiv.), ethyl bromide (22·3 g., 1 mol.), sodium as before, and 2-ethoxyethyl iodide (41·0 g., 1 mol.), gave the *phosphine* (IX) (27·0 g., 63%), b. p. 141—149°/18 mm. (Found, for a refractionated sample, b. p. 146·5°/18 mm.: C, 68·7; H, 9·1. $C_{12}H_{19}OP$ requires C, 68·5; H, 9·1%).

A solution of the phosphine (IX) (30·5 g.) in acetic acid (400 c.c.) was boiled under reflux in nitrogen whilst hydrogen bromide was passed through it for 8 hr., and the solvent was then evaporated under reduced pressure. The residual crude hydrobromide of 2-bromoethyl-ethylphenylphosphine (X) was shaken in nitrogen with a mixture of chloroform and air-free aqueous sodium hydrogen carbonate. Evaporation of the dried chloroform extract gave the liquid phosphine (X) (*ca.* 70%), which in toluene solution, after 2 hours' boiling, gave the dibromide (VIII), decomposing at *ca.* 370° (Found: C, 49·3; H, 6·1%); this gave the dipicrate, m. p. and mixed m. p. 240—245° (decomp.) (Found: C, 48·6; H, 4·5; N, 11·0%). Samples of the free phosphine, when set aside under nitrogen, underwent spontaneous but erratic self-quaternisation: a sample heated to *ca.* 110° underwent such vigorous exothermic quaternisation that partial decomposition reduced the yield of the dibromide (VIII) to 30%.

[7] Davies and Lewis, *J.*, 1934, 1599.

XUM

Thermal Decomposition of the Dibromide (VIII).—A mixture of the dibromide and anhydrous potassium carbonate was placed in a small distillation flask, the side-arm of which was fitted directly into a similar flask to permit subsequent direct refractionation of the initial crude distillate. The mixture was then heated in nitrogen at 360—370°/10 mm. for 2 hr. The clear limpid distillate, when refractionated, gave the diphosphine (VII), b. p. 160—175°/1 mm., m. p. and mixed m. p. 67—70°, after crystallisation from ethanol (Found: C, 71·7; H, 8·4%); it gave the dimethiodide, m. p. and mixed m. p. 199—200°, after crystallisation from methanol.

Alternatively, the pure dibromide (VIII), when heated in a tube in nitrogen at 360—370°/10 mm., gave a hard yellow sublimate, undoubtedly of the dihydrobromide of the diphosphine (VII). The powdered sublimate was shaken with benzene and aqueous sodium hydrogen carbonate, and the benzene extract, when dried and distilled, gave the diphosphine (VII), b. p. 162—163°/0·5 mm., m. p. and mixed m. p. 70—71° after crystallisation from ethanol.

2-*Bromoethyltriethylphosphonium Bromide* (XI).—A mixture of triethylphosphine (5·1 g.), ethylene dibromide (40·5 g., 5 mols.), and ethanol (4 c.c.) was set aside under nitrogen for 2 days and then boiled under reflux for 1 hr. After removal of the solvent, the residue was washed with ether and recrystallised from ethanol, affording the deliquescent bromide (5·5 g., 42%), m. p. *ca.* 235° (decomp.) (lit.,[8] 235°) (Found: C, 30·9; H, 6·5. Calc. for $C_8H_{19}Br_2P$: C, 31·4; H, 6·3%).

The bromide (4 g.), when heated at 325°/20 mm. in nitrogen for 2 hr., gave no distillate, although hydrogen bromide (0·6 mol.) collected in a liquid-nitrogen trap. The charred residue (2·5 g.) could not be purified or converted into a satisfactory derivative.

A mixture of triethylphosphine (5 g.), 2-ethoxyethyl bromide (7·1 g., 1·1 mols.), and ethanol (5 c.c.) was boiled under reflux in nitrogen for 2 hr., and the solvent removed. The residual bromide (XII; R = Et) was too deliquescent for recrystallisation: heating it in nitrogen at 0·1 mm. gave no distillate at 250°, and increasing the temperature to 400° caused only slow charring. The bromide (XII; R = Ph), a highly deliquescent salt prepared in the same way, behaved similarly on being heated.

s-*Ethylenebis(triethylphosphonium) Dibromide* (XIII; R = Et).—Triethylphosphine (5·0 g.), ethylene dibromide (3·2 g., 0·4 mol.), and ethanol were heated under nitrogen in a sealed tube at 100° for 15 hr. The hygroscopic dibromide (6·6 g., 92%) precipitated with ether and recrystallised from ethanol had m. p. 260° (decomp.) (Found: C, 38·8; H, 8·2. Calc. for $C_{14}H_{34}Br_2P_2$: C, 39·6; H, 8·1%); it gave a yellow *dipicrate*, m. p. 208—210° (from much ethanol) (Found: C, 43·7; H, 5·3; N, 11·5. $C_{26}H_{28}O_{14}N_6P_2$ requires C, 43·3; H, 5·3; N, 11·7%).

The dibromide, when heated in nitrogen at 0·1 mm. with a brush flame, or at 350°/15 mm., gave triethylphosphine (*ca.* 40%) as its hydrobromide. The free phosphine was identified (*a*) by precipitation from ethanolic solution of its yellow *picrate*, m. p. 106—107° (decomp.) (from ethanol) (Found: C, 41·0; H, 5·3; N, 12·3. $C_6H_{15}P,C_6H_3O_7N_3$ requires C, 41·5; H, 5·2; N, 12·1%), (*b*) as its ethiodide, m. p. 293—297° (decomp.) (Found: C, 35·1; H, 7·7. Calc. for $C_8H_{20}IP$: C, 35·0; H, 7·4%), (*c*) as the yellow dichlorodiphosphinepalladium, m. p. 137—138° (lit.,[9] 139°) (Found: C, 35·0; H, 7·0. Calc. for $C_{12}H_{30}Cl_2P_2Pd$: C, 34·8; H, 7·3%), and (*d*) as the pale orange *dibromodiphosphinepalladium*, m. p. 131—132° (from ethanol) (Found: C, 28·7; H, 5·4. $C_{12}H_{30}Br_2P_2Pd$ requires C, 28·7; H, 6·0%). These derivatives, when mixed with authentic samples, underwent no change in m. p.

Hofmann [8] showed that the dihydroxide corresponding to the dibromide (XIII; R = Et) when heated yielded triethylphosphine, its oxide, and ethylene.

s-*Ethylenebis(diethylphenylphosphonium) Dibromide* (XIII; R = Ph).—This *salt* was prepared (*a*) in 78% yield by heating a mixture of ethylene dibromide and diethylphenylphosphine (2 mols.) in a sealed tube in nitrogen at 160° for 2 hr., and (*b*) in 57% yield by boiling this mixture diluted with ethanol under reflux in nitrogen for 5 hr. It had m. p. 257—259° (decomp.) after crystallisation from ethanol (Found: C, 50·5; H, 6·3. $C_{22}H_{34}Br_2P_2$ requires C, 50·8; H, 6·6%) and gave a yellow *dipicrate*, m. p. 188—190° (decomp.) (Found: C, 49·5; H, 5·0; N, 10·5. $C_{34}H_{38}O_{14}N_6P_2$ requires C, 50·0; H, 4·7; N, 10·3%). The dibromide was apparently unaffected when heated at 310°/0·1 mm. for even 20 hr. Heating at 350°/0·001 mm. or at 360°/12 mm., caused charring with distillation of a liquid which on cooling formed the waxy solid diethylphenylphosphine hydrobromide. The liberated phosphine was identified as its

[8] Hofmann, *Phil. Trans.*, 1860, **150**, 409; *Annalen*, 1861, *Suppl. I*, **156**, 275.
[9] Mann and Purdie, *J.*, 1935, 1549.

XUM

ethobromide, m. p. 184—186° (from ethanol) (lit.,[7] 187—188°), and as the dibromodiphosphinepalladium, m. p. and mixed m. p. 132—133° (from ethanol).

s-Trimethylenebis(triethylphosphonium) dibromide was prepared as (XIII; R = Et) in 88% yield as deliquescent crystals, m. p. *ca.* 260° (decomp.) (Found: C, 40·8; H, 8·7. $C_{15}H_{36}Br_2P_2$ requires C, 41·1; H, 8·3%). When heated at 345°/15 mm. it gave triethylphosphine (*ca.* 30%), identified as the above ethiodide and dichloro- and dibromo-diphosphinepalladium.

Di-(2-ethoxyethyl)phenylphosphine (XIV; R = OEt).—Phenylphosphine (9·3 g.) in liquid ammonia (150 c.c.) was treated in turn with sodium (1·9 g., 1 equiv.) and 2-ethoxyethyl iodide (16·8 g., 1 mol.), and then again with these reagents in this order. After evaporation of the ammonia, distillation in nitrogen gave the *phosphine* (13·5 g., 64%), b. p. 118—122°/0·5 mm. (Found: C, 66·4; H, 9·3. $C_{14}H_{23}O_2P$ requires C, 66·1; H, 9·1%). It readily afforded pale orange *dibromobis[di-(2-ethoxyethyl)phenylphosphine]palladium*, m. p. 111—112° (from ethanol) (Found: C, 43·3; H, 6·2. $C_{28}H_{46}O_4Br_2P_2Pd$ requires C, 43·4; H, 6·0%).

A mixture of phenylphosphine (5·2 g.) and ethylene oxide (4·6 g., 2·2 mols.) under nitrogen, when heated in a sealed tube at 100° for 5 hr., afforded on distillation an almost quantitative recovery of the phosphine. Heating at 100° for 18 hr. gave a gum; attempted distillation up to 200°/0·2 mm. gave a negligible distillate, and the residue was insoluble in all the usual solvents.

Many attempts were made to hydrogenate acetylenebis(diphenylphosphine), $Ph_2P{\cdot}C{\equiv}C{\cdot}PPh_2$,[10] directly or indirectly, and thus ultimately obtain *s*-ethylenebis(diphenylphosphine) (as VII). All hydrogenating metallic catalysts were, as expected, rapidly poisoned and rendered inert by the diphosphine, which was subsequently recovered. Other reducing agents were either without effect or gave crude products from which no pure compound could be isolated. Similar results were obtained with acetylenebis(diphenylarsine).[11]

We are greatly indebted to Imperial Chemical Industries Limited, Pharmaceuticals Division, for the therapeutic tests, to Dr. F. H. C. Stewart for assistance in the preparation of the dibromide (XIII; R = Ph), and to the Department of Scientific and Industrial Research for a grant (to C. H. S. H.).

University Chemical Laboratory, Cambridge. [*Received, January 23rd,* 1958.]

[10] Hartmann, Beermann, and Czempik, *Z. anorg. Chem.*, 1956, **287**, 261.
[11] *Idem, Angew. Chem.*, 1955, **67**, 233.

---

430. *Cyclic Amidines. Part VII.* Preparation of Benziminazoles from N′-Aryl-N-hydroxyamidines.*

By M. W. Partridge and H. A. Turner.

2-Substituted benziminazoles can be prepared by treatment of an *N′*-aryl-*N*-hydroxyamidine with benzenesulphonyl chloride and a tertiary base under anhydrous conditions. A naphth[1,2]iminazole can be made in this way. In the presence of aqueous alkali, an *N′*-aryl-*N*-hydroxyamidine and benzenesulphonyl chloride afford an *NN′*-disubstituted urea.

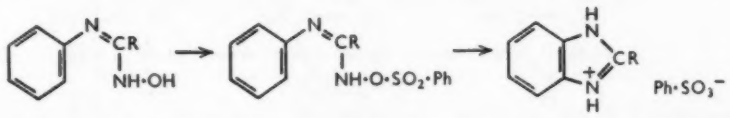
1 : 2-Disubstituted benzene derivatives in which the nitrogen atoms of the two functional groups are attached directly to the nucleus have hitherto been employed for the production of benziminazoles. Alternatively the appropriate 1 : 2-disubstituted benzene has been produced by a rearrangement of the Beckmann,[1] Curtius,[2] or Lossen [3]

* Part VI, *J.*, 1958, 614.

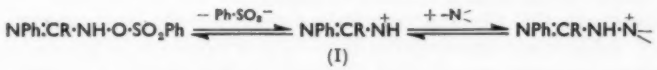
[1] Auwers and Meyenburg, *Ber.*, 1891, **24**, 2370.
[2] Lindemann and Schultheis, *Annalen*, 1928, **464**, 237.
[3] Scott and Wood, *J. Org. Chem.*, 1942, **7**, 508.

type. Pellizzari and Gaiter [4] have however prepared 2-cyanamido-1-cyanobenziminazole from *N*-cyano-*N*-phenylhydrazine and cyanogen bromide.

We have found that 2-substituted benziminazoles are readily produced when an *N'*-aryl-*N*-hydroxyamidine is brought into reaction under anhydrous conditions with benzenesulphonyl chloride in the presence of pyridine or triethylamine:

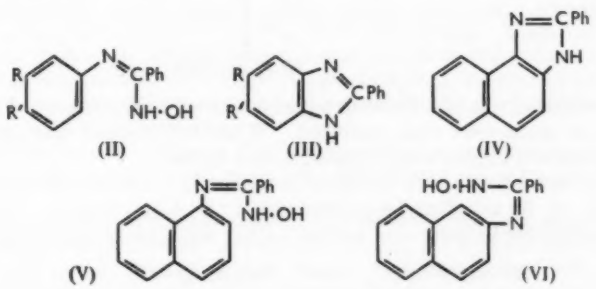


It is possible that the cyclisation involves the intermediate production of a strongly electrophilic imidinium cation (I), resulting from the tendency of the oxime ester to ionise, and being partially stabilised by the organic base:



(I)

Rearrangement of the oxime was not observed even when the reaction was carried out in the hot. The process recalls the cyclisation of sulphonyl esters of 4-arylbutan-2-one oximes [5] to yield products formulated as *iso*quinoline derivatives, since it was considered that the ester underwent a Beckmann transformation before cyclisation; the formation of quinolines has however been observed in analogous reactions.[6]



(II) (III) (IV) (V) (VI)

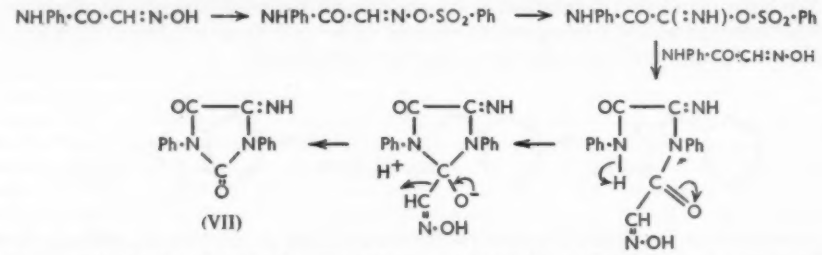
The orientation of the *Bz*-alkylated benziminazoles described in the Experimental section followed from the orientation of the *N'*-aryl-*N*-hydroxyamidine or was established by comparison with authentic specimens prepared from the appropriate *o*-phenylenediamine. Both *N*-hydroxy-*N'*-3-methyl- (II; R = Me, R' = H) and *N*-hydroxy-*N'*-4-methyl-phenylbenzamidine (II; R = H, R' = Me) afforded 5-methyl-2-phenylbenziminazole (III; R = Me, R' = H); and *N'*-3 : 4-dimethylphenyl-*N*-hydroxybenzamidine (II; R = R' = Me) gave 5 : 6-dimethyl-2-phenylbenziminazole (III; R = R' = Me). 2-Phenylnaphth[1,2]iminazole (IV) was obtained from both *N*-hydroxy-*N'*-1- (V) and -2-naphthylbenzamidine (VI).

α-Hydroxyiminoacetanilide, treated in the same way, furnished 4-imino-1 : 3-diphenylparabanic acid (VII) which was identified by hydrolysis to 1 : 3-diphenylparabanic acid and to diphenylurea. It is supposed that the oxime sulphonate, after rearrangement, afforded the parabanic acid by reaction with unchanged α-hydroxyiminoacetanilide

[4] Pellizzari and Gaiter, *Gazzetta*, 1918, **48**, 151.
[5] Scheuing and Walach, G.P. 576,532; 579,227/1933.
[6] Burstin, *Monatsh.*, 1913, **34**, 1443.

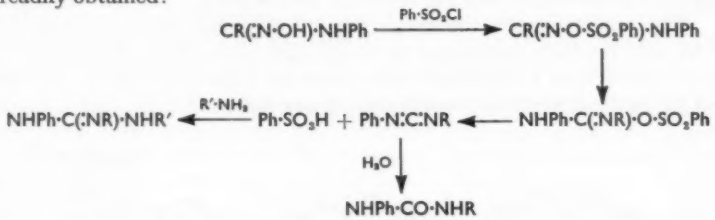
XUM

involving a process reminiscent of the fission of 2-2′-hydroxyiminoacylfurans to aldoximes and furoic esters, and of α-nitroso-ketones: [7]



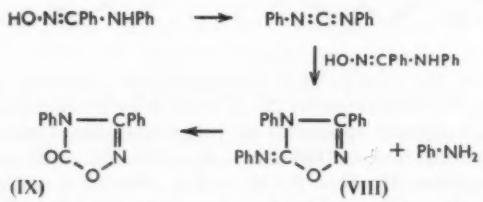
The required *N*-aryl-*N*′-hydroxyamidines, not hitherto described, were prepared by treatment with hydroxylamine of *N*-arylamidines which were themselves obtained by the sulphonate fusion [8] or aluminium chloride [9] method.

By analogy with the Tiemann reaction in which a cyanamide is produced from an amidoxime,[10] it had been expected that an *N*′-aryl-*N*-hydroxyamidine on treatment with benzenesulphonyl chloride would afford a carbodi-imide from which a urea or a guanidine could be readily obtained:



This series of reactions was effected with aqueous sodium hydroxide as acid-binding agent, and a number of ureas were thus produced. When the reaction was carried out in the presence of an amine a trisubstituted guanidine was formed.

Collateral evidence for the intermediate formation of a carbodi-imide was provided by the formation of 3 : 4-diphenyl-5-phenylimino-1 : 2 : 4-oxadiazoline (VIII) when *N*-hydroxy-*N*′-phenylbenzamidine was treated either with benzenesulphonyl chloride and

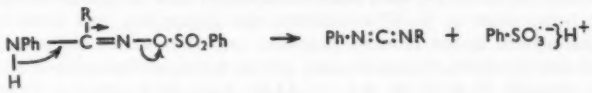


sodium ethoxide in ethanol, or with diphenylcarbodi-imide. This 5-phenylimino-oxadiazoline (VIII) was readily hydrolysed to the known, corresponding 5-oxo-oxadiazoline (IX) which was also formed, together with diphenylurea and *N*-phenylbenzamidine, when the same substituted amidoxime was treated with benzenesulphonyl chloride and potassium carbonate in acetone.

Attempts to isolate a benzenesulphonyl ester of these *N*′-aryl-*N*-hydroxyamidines were

[7] Monoya, *J. Pharm. Soc. Japan*, 1919, **447**, 357; Asahina and Murayama, *Arch. Pharm.*, 1914, **252**, 435; Woodward and Doering, *J. Amer. Chem. Soc.*, 1945, **67**, 860.
[8] Oxley and Short, *J.*, 1946, 147.
[9] Oxley, Partridge, and Short, *J.*, 1947, 1110.
[10] Tiemann, *Ber.*, 1891, **24**, 4162; Partridge and Turner, *J. Pharm. Pharmacol.*, 1953, **5**, 103.

unsuccessful, and no evidence was found of the intervention of an imidosulphonate [NHPh·C(:NR)·O·SO_2Ph] in this series of reactions. Indeed the reactions leading to the formation of ureas occurred with such facility that the elimination of the benzenesulphonate anion and a proton may be concerted with the rearrangement:



Experimental

N-2 : 3-*Dimethylphenylbenzamidine*.—Equimolecular quantities of 2 : 3-dimethylaniline, anhydrous toluene-*p*-sulphonic acid, and phenyl cyanide were heated together at 180° for 5 hr. The cooled melt was powdered, washed with ether, basified by trituration with aqueous sodium hydroxide, washed with water, and crystallised from ethanol; this *amidine* had m. p. 130° (Found: N, 12·1. $C_{15}H_{16}N_2$ requires N, 12·5%); yield 79%. Its *toluene*-p-*sulphonate*, m. p. 165°, crystallised from aqueous ethanol (Found: N, 6·9. $C_{22}H_{24}O_3N_2S$ requires N, 7·1%); the *picrate* formed prisms, m. p. 174—175°, from ethanol (Found: N, 15·3. $C_{21}H_{19}O_7N_5$ requires N, 15·5%). By the aluminium chloride method (see below), the yield was 73%.

The following amidines were prepared in a similar manner:

N-2 : 4-Dimethylphenplbenzamidine (39%), m. p. 112° (Lottermoser [11] records m. p. 107—108°) (Found: N, 12·6. Calc. for $C_{15}H_{16}N_2$: N, 12·5%). By the aluminium chloride method, the amidine was prepared in 51% yield.

N-2 : 5-*Dimethylphenylbenzamidine* (41%), m. p. 132° (Found: C, 80·2; H, 7·0. $C_{15}H_{16}N_2$ requires C, 80·3; H, 7·2%) [*picrate*, m. p. 191—192° (Found: C, 56·0; H, 3·9. $C_{21}H_{19}O_7N_5$ requires C, 55·6; H, 4·2%)].

N-3 : 4-*Dimethylphenylbenzamidine*.—Powdered aluminium chloride (27 g.) was gradually stirred into a mixture of 3 : 4-dimethylaniline (24 g., 1 mol.) and phenyl cyanide (21 g., 1 mol.) during 20 min. and the mixture was then heated at 180° for 20 min. A solution of the product in ethanol was made strongly alkaline with aqueous sodium hydroxide and extracted with chloroform. After being washed with water and dried (K_2CO_3), the chloroform solution gave the *amidine* which, after crystallisation from light petroleum, had m. p. 94° (Found: N, 12·8. $C_{15}H_{16}N_2$ requires N, 12·5%); yield 29 g.

N-m-*Tolylbenzamidine* was prepared (72%) analogously to the foregoing compound and, after crystallisation from benzene, had m. p. 105—106° (Found: N, 13·4. $C_{14}H_{14}N_2$ requires N, 13·3%).

N-*Hydroxy*-N′-p-*methoxyphenylbenzamidine*.—*N*-*p*-Methoxyphenylbenzamidine (23 g.) was added to a solution of hydroxylamine hydrochloride (10·4 g., 1·5 mols.) in water (90 ml.). The suspension was boiled for 10 min., made just alkaline to Brilliant-yellow with ammonia, and boiled for a further 10 min. The solid which separated furnished the pure *amidoxime*, as plates, m. p. 121—122°, on recrystallisation from ethanol (yield 10 g.) (Found: N, 11·6. $C_{14}H_{14}O_2N_2$ requires N, 11·6%). Its *benzoyl derivative*, prepared under Schotten–Baumann conditions, had m. p. 105° after recrystallisation from aqueous ethanol (Found: N, 8·3. $C_{21}H_{18}O_3N_2$ requires N, 8·1%).

The following amidoximes were analogously prepared from the appropriate *N*-arylamidine and hydroxylamine: N-*Hydroxy*-N′-m-*tolylbenzamidine* (60%), m. p. 138° (Found: N, 12·6. $C_{14}H_{14}ON_2$ requires N, 12·4%); N′-2 : 3-*dimethylphenyl*-N-*hydroxybenzamidine* (83%), m. p. 195—196° (Found: C, 74·9; H, 6·7; N, 11·6. $C_{15}H_{16}ON_2$ requires C, 75·0; H, 6·7; N, 11·7%); N′-2 : 4-*dimethylphenyl*-N-*hydroxybenzamidine* (42%), m. p. 142° (Found: N, 11·9. $C_{15}H_{16}ON_2$ requires N, 11·7%); N′-2 : 5-*dimethylphenyl*-N-*hydroxybenzamidine* (39%), m. p. 144° (Found: C, 75·3; H, 6·5; N, 11·4. $C_{15}H_{16}ON_2$ requires C, 75·0; H, 6·7; N, 11·7%); N′-3 : 4-*dimethylphenyl*-N-*hydroxybenzamidine* (30%), needles, m. p. 137—138°, from light petroleum (Found: N, 11·9. $C_{15}H_{16}ON_2$ requires N, 11·7%); when the foregoing compound was prepared in aqueous ethanol, the yield was 60%. N-*Hydroxy*-N′-*phenyl*-α-*phenylacetamidine* (47%), m. p. 140—141° (Found: N, 12·5. $C_{14}H_{14}ON_2$ requires N, 12·4%); N-*hydroxy*-N′-1-*naphthylbenzamidine* (79%), m. p. 183° (Found: N, 10·4. $C_{17}H_{14}ON_2$ requires N, 10·7%); this preparation was carried out in aqueous ethanol and heating was continued for 2 hr.

[11] Lottermoser, *J. prakt. Chem.*, 1896, **54**, 127.

XUM

N-*Hydroxy*-N′-2-*naphthylbenzamidine* (41%), m. p. 181—182°, depressed to about 160° by the foregoing compound (Found: N, 10·7%).

2-*Phenylbenziminazole*.—(i) *N*-Hydroxy-*N*′-phenylbenzamidine (0·025 mole), dissolved in a mixture of dry benzene (20 ml.) with dry pyridine (10 ml.) or dry triethylamine (10 ml.), was treated during 30 min. at below 10° with benzenesulphonyl chloride (0·025 mole), in dry benzene (10 ml.). After being kept at 0—5° overnight, the suspension was filtered. Solvent was removed from the filtrate under reduced pressure, and the residue triturated with aqueous sodium carbonate and crystallised from ethanol, giving 2-phenylbenziminazole (88%), m. p. and mixed m. p. 288° (Found: C, 80·0; H, 5·1; N, 14·6. Calc. for $C_{13}H_{10}N_2$: C, 80·4; H, 5·2; N, 14·4%). The benzene-insoluble material, after being washed with water and crystallised from aqueous ethanol, afforded 2-*phenylbenziminazole benzenesulphonate* (10%), m. p. 262° (Found: C, 64·4; H, 4·5; N, 7·8. $C_{19}H_{16}O_3N_2S$ requires C, 64·8; H, 4·6; N, 8·0%) [derived *toluene*-p-*sulphonate*, m. p. 196°, from aqueous ethanol (Found: N, 7·8. $C_{20}H_{18}O_3N_2S$ requires N, 7·7%)].

(ii) When the foregoing reaction was carried out in boiling benzene during 40 min., the yield of 2-phenylbenziminazole was 58%.

The following benziminazole derivatives were prepared and purified analogously from the named *N*′-aryl-*N*-hydroxyamidine, benzenesulphonyl chloride, and pyridine or triethylamine.

4-Methyl-2-phenylbenziminazole (from *N*-hydroxy-*N*′-*o*-tolylbenzamidine [12]) (90%), m. p. 251—252°, from aqueous ethanol (Found: C, 81·1; H, 5·6; N, 13·6. Calc. for $C_{14}H_{12}N_2$: C, 80·7; H, 5·8; N, 13·5%) (Montanari and Passerini [13] record m. p. 246°) [*benzenesulphonate*, m. p. 210—212°, from aqueous ethanol (Found: C, 65·9; H, 4·7; N, 7·9. $C_{20}H_{18}O_3N_2S$ requires C, 65·6; H, 5·0; N, 7·7%); *picrate*, m. p. 237—238°, from acetic acid (Found: C, 55·2; H, 3·6; N, 16·3. $C_{20}H_{15}O_7N_5$ requires C, 54·9; H, 3·5; N, 16·0%)].

5-Methyl-2-phenylbenziminazole, (i) (from *N*-hydroxy-*N*′-p-tolylbenzamidine [14]) (63%), m. p. 246°, from benzene (Found: C, 80·9; H, 5·9. Calc. for $C_{14}H_{12}N_2$: C, 80·7; H, 5·8%) (Green and Day [15] give m. p. 249—250°) [*benzenesulphonate*, m. p. 236—237°, from ethanol (Found: N, 7·4. $C_{20}H_{18}O_3N_2S$ requires N, 7·7%); *picrate*, m. p. 265°, from aqueous acetic acid (Found: N, 16·0. $C_{20}H_{15}O_7N_5$ requires N, 16·0%)]. (ii) (From *N*-hydroxy-*N*′-*m*-tolylbenzamidine) (91%), m. p. 244°, undepressed on admixture with the foregoing specimen or with a sample obtained from the interaction of equivalent quantities of 3 : 4-diaminotoluene, phenyl cyanide, and ammonium benzenesulphonate at 200° for 4 hr.

4 : 5-*Dimethyl*-2-*phenylbenziminazole* (from *N*′-2 : 3-dimethylphenyl-*N*-hydroxybenzamidine) (62%), m. p. 204°, from benzene–light petroleum (Found: C, 81·1; H, 6·4; N, 12·3. $C_{15}H_{14}N_2$ requires C, 81·1; H, 6·4; N, 12·6%) [*benzenesulphonate*, m. p. 225—226°, from ethanol (Found: N, 7·4. $C_{21}H_{20}O_3N_2S$ requires N, 7·4%)].

4 : 6-Dimethyl-2-phenylbenziminazole (from *N*′-2 : 4-dimethylphenyl-*N*-hydroxybenzamidine) (65%), m. p. 196°, from benzene–light petroleum (Found: C, 80·9; H, 6·4; N, 12·8. Calc. for $C_{15}H_{14}N_2$: C, 81·1; H, 6·4; N, 12·6%) (Hübner [16] gives m. p. 195°) [*benzenesulphonate*, m. p. 177—178°, from aqueous ethanol (Found: N, 7·1. $C_{21}H_{20}O_3N_2S$ requires N, 7·4%); *picrate*, m. p. 258—259°, from aqueous acetic acid (Found: N, 15·2. $C_{21}H_{17}O_7N_5$ requires N, 15·5%)].

4 : 7-Dimethyl-2-phenylbenziminazole (from *N*′-2 : 5-dimethylphenyl-*N*-hydroxybenzamidine) (64%), m. p. 240°, from benzene–light petroleum (Found: C, 80·7; H, 6·5; N, 12·7. Calc. for $C_{15}H_{14}N_2$: C, 81·1; H, 6·4; N, 12·6%) (Hübner [16] records m. p. 215°) [*benzenesulphonate*, m. p. 278—279°, from ethanol (Found: C, 66·2; H, 5·6; N, 7·1. $C_{21}H_{20}O_3N_2S$ requires C, 66·3; H, 5·3; N, 7·4%); *picrate*, m. p. 254°, from ethanol (Found: C, 55·5; H, 4·0; N, 15·5. $C_{21}H_{17}O_7N_5$ requires C, 55·8; H, 3·8; N, 15·5%)].

5 : 6-Dimethyl-2-phenylbenziminazole (from *N*′-3 : 4-dimethylphenyl-*N*-hydroxybenzamidine) (36%), m. p. 254—255°, from light petroleum, undepressed by a specimen produced from the reaction between 4 : 5-dimethylphenylene-1 : 2-diamine, phenyl cyanide, and ammonium benzenesulphonate at 200° for 4 hr. (Davies, Mamalis, Petrow, and Sturgeon [17] record m. p. 251—252°) [*benzenesulphonate*, m. p. 281—282°, from ethanol (Found: C, 65·9; H, 5·2; N, 7·4.

[12] Ley, *Ber.*, 1898, **31**, 240.
[13] Montanari and Passerini, *Boll. sci. Fac. Chim. ind. Bologna*, 1953, **11**, 42.
[14] Müller, *Ber.*, 1889, **22**, 2401.
[15] Green and Day, *J. Amer. Chem. Soc.*, 1942, **64**, 1167.
[16] Hübner, *Annalen*, 1881, **208**, 278.
[17] Davis, Mamalis, Petrow, and Sturgeon, *J. Pharm. Pharmacol.*, 1951, **3**, 420.

XUM

$C_{21}H_{20}O_3N_2S$ requires C, 66·3; H, 5·3; N, 7·4%); *picrate*, m. p. 284° from acetic acid (Found: N, 15·3. $C_{21}H_{17}O_7N_5$ requires N, 15·5%)].

5-Methoxy-2-phenylbenziminazole (from *N*-hydroxy-*N'*-4-methoxyphenylbenzamidine) (69%), m. p. 147°, from benzene–light petroleum (Found: N, 12·5. Calc. for $C_{14}H_{12}ON_2$: N, 12·5%) (Poraĭ-Koshits, Efros, and Ginzburg [18] record m. p. 142°) [*picrate*, m. p. 237°, from ethanol (Found: N, 15·3. $C_{20}H_{15}O_8N_5$ requires N, 15·5%)].

5-Chloro-2-phenylbenziminazole (from *N'*-*p*-chlorophenyl-*N*-hydroxybenzamidine [12]) (90%), m. p. 210°, from benzene (Found: N, 12·3. Calc. for $C_{13}H_9N_2Cl$: N, 12·3%) (Fischer and Limmer [19] give m. p. 210°) [*benzenesulphonate*, m. p. 242°, from ethanol (Found: N, 7·0. $C_{19}H_{15}O_3N_2ClS$ requires N, 7·2%); *picrate*, m. p. 246—248°, from ethanol (Found: N, 15·4. $C_{19}H_{12}O_7N_5Cl$ requires N, 15·3%)].

2-Phenylnaphth[1,2]iminazole (i) (from *N*-hydroxy-*N'*-1-naphthylbenzamidine) (96%), m. p. 218°, from benzene (Found: N, 11·4. Calc. for $C_{17}H_{12}N_2$: N, 11·5%) (Hunter [20] gives m. p. 218°) [*picrate*, m. p. 260°, from aqueous acetic acid (Found: N, 14·8. $C_{23}H_{15}O_7N_5$ requires N, 14·8%)]; (ii) (from *N*-hydroxy-*N'*-2-naphthylbenzamidine) (75%), m. p. 217—218°, undepressed on admixture with the foregoing naphthiminazole.

2-Methylbenziminazole (from *N*-hydroxy-*N'*-phenylacetamidine [14]) (80%), m. p. 174—175°, undepressed by an authentic specimen.[21]

2-Benzylbenziminazole (from *N*-hydroxy-*N'*-phenyl-α-phenylacetamidine) (63%), m. p. 188—189°, from aqueous ethanol, undepressed by an authentic specimen [22] (Found: C, 81·2; H, 5·9. Calc. for $C_{14}H_{12}N_2$: C, 80·7; H, 5·8%).

4-*Imino*-1 : 3-*diphenylparabanic Acid*.—α-Hydroxyiminoacetanilide (4·9 g.), suspended in a mixture of dry ether (120 ml.) and triethylamine (6 g.), was treated at 5—10° with benzenesulphonyl chloride (5·3 g.). Next day, the suspension was filtered and evaporated. The parabanic acid (2·3 g.) crystallised when the gummy residue was stirred with propan-2-ol and, after crystallisation from ethanol, had m. p. 136—137° [Found: C, 68·2; H, 4·1; N, 15·5%; *M* (Rast), 251. Calc. for $C_{15}H_{11}O_2N_3$: C, 67·9; H, 4·2; N, 15·8%; *M*, 265]; Dieckmann and Kämmerer [23] record m. p. 137°. On hydrolysis with hydrochloric acid, the above compound afforded 1 : 3-diphenylparabanic acid, m. p. 204—206° (Found: C, 68·0; H, 3·8. Calc. for $C_{15}H_{10}O_3N_2$: C, 67·7; H, 3·8%); Dieckmann *et al.*[23] give m. p. 204°. Hydrolysis with aqueous alkali gave diphenylurea, m. p. and mixed m. p. 238—239°.

Diarylureas from N'-Aryl-N-hydroxybenzamidines.—To a suspension of the amidine (0·025 mole) in water (20 ml.), benzenesulphonyl chloride (0·025 mole) and 2N-sodium hydroxide (30 ml.) were gradually added with stirring and external cooling; the reaction was exothermic. Stirring was continued for 3 hr., the solid was collected, washed with water, and crystallised from ethanol.

The following ureas were thus prepared: *NN'*-Diphenyl- (69%), m. p. and mixed m. p. 237°; *N*-*p*-chlorophenyl-*N'*-phenyl- (72%), m. p. and mixed [24] m. p. 238—239°; *N*-phenyl-*N'*-*p*-tolyl- (57%), m. p. and mixed [24] m. p. 212—213°; N-2 : 3-*dimethylphenyl*-N'-*phenyl*- (83%), m. p. 189°, undepressed by a specimen prepared from phenyl *iso*cyanate and 2 : 3-dimethylaniline (Found: C, 75·1; H, 6·9; N, 11·8. $C_{15}H_{16}ON_2$ requires C, 75·0; H, 6·7; N, 11·7%); *N*-2 : 4-dimethylphenyl-*N'*-phenyl- (80%), m. p. 242°, undepressed by a sample prepared from phenyl *iso*cyanate and 2 : 4-dimethylaniline (Manuelli and Comanducci [25] record m. p. 242—243°); N-2 : 5-*dimethylphenyl*-N'-*phenyl*- (62%), m. p. 234° (Found: C, 74·9; H, 6·7. $C_{15}H_{16}ON_2$ requires C, 75·0; H, 6·7%).

NN'-*Diphenyl*-N''-o-*tolylguanidine*.—To a stirred suspension of *N*-hydroxy-*N'*-*o*-tolylbenzamidine [12] (4·5 g.) and aniline (1·9 g.) in 5N-sodium hydroxide (10 ml.), benzenesulphonyl chloride (7·1 g.) was added dropwise. After 3 hr. the suspension was filtered. The filtrate on acidification gave benzenesulphonanilide (1·9 g.), m. p. and mixed m. p. 112°. Basic material was extracted from the residue with dilute hydrochloric acid, liberated, collected in chloroform, and recovered; on crystallisation from ethanol, this afforded the guanidine (1 g.), m. p. 110°

[18] Poraĭ-Koshits, Efros, and Ginzburg, *J. Gen. Chem.* (*U.S.S.R.*), 1949, **19**, 1545.
[19] Fischer and Limmer, *J. prakt. Chem.*, 1906, **74**, 57.
[20] Hunter, *J.*, 1945, 806.
[21] Phillips, *J.*, 1928, 172.
[22] Walther and Pulawski, *J. prakt. Chem.*, 1899, **59**, 249.
[23] Dieckmann and Kämmerer, *Ber.*, 1905, **38**, 2977.
[24] Ingold, *J.*, 1924, **125**, 87.
[25] Manuelli and Comanducci, *Gazzetta*, 1899, **29**, 143.

XUM

(Found: C, 79·7; H, 6·6; N, 14·2. Calc. for $C_{20}H_{18}N_2$: C, 79·9; H, 6·4; N, 13·9%); Marckwald [26] records m. p. 112°. Its nitrate had m. p. 174° (Marckwald [26] gives m. p. 172°). The non-basic fraction gave on repeated crystallisation from aqueous ethanol *N*-phenyl-*N'*-*o*-tolylurea (2·3 g.), m. p. and mixed m. p. 193—194°.

NN'N''-Triphenylguanidine (7%) together with *NN'*-diphenylurea (14%) were produced analogously from *N*-hydroxy-*N'*-phenylbenzamidine.

3 : 4-*Diphenyl*-5-*phenylimino*-1 : 2 : 4-*oxadiazoline*.—(i) *N*-Hydroxy-*N'*-phenylbenzamidine (4·2 g.) was added to a solution from sodium (0·5 g., 1·1 at.) in ethanol (30 ml.); benzenesulphonyl chloride (3·5 g., 1 mol.) in ethanol (50 ml.) was added at 10—15°. Next day the solution was boiled for 30 min. The separated solid gave the *oxadiazoline* (3 g.), m. p. 159—160°, on crystallisation from ethanol (Found: C, 76·9; H, 4·7; N, 13·4. $C_{20}H_{15}ON_3$ requires C, 76·7; H, 4·8; N, 13·4%).

(ii) A solution of *N*-hydroxy-*N'*-phenylbenzamidine (4·2 g.), diphenylcarbodi-imide (4 g., 1 mol.) and triethylamine (4 drops) in anhydrous benzene (100 ml.) was kept overnight, boiled for 30 min., concentrated, and mixed with ethanol. The precipitate (5·7 g.) gave the same oxadiazoline, m. p. and mixed m. p. 159—160°.

5-*Oxo*-3 : 4-*diphenyl*-1 : 2 : 4-*oxadiazoline*.—(i) The foregoing 5-phenylimino-1 : 2 : 4-oxadiazoline (0·5 g.) was boiled with concentrated hydrochloric acid (7 ml.) for 30 min. The precipitate gave the 5-oxo-1 : 2 : 4-oxadiazoline (0·35 g.), m. p. 167—168° (from ligroin), undepressed by a sample prepared by Müller's method [27] (Found: C, 70·7; H, 4·1; N, 11·8. Calc. for $C_{14}H_{10}O_2N_2$: C, 70·6; H, 4·2; N, 11·8%).

(ii) *N*-Hydroxy-*N'*-phenylbenzamidine (5·3 g.), benzenesulphonyl chloride (4·4 g.), and potassium carbonate (3·5 g.) were refluxed together for 2 hr. in acetone (40 ml.) which had been freed from oxidisable matter. Solvent was removed from the filtered suspension; an aqueous lactic acid extract of the tarry residue furnished on basification *N*-phenylbenzamidine (0·35 g.), m. p. and mixed m. p. 113—114°. The non-basic tar on fractional crystallisation from aqueous ethanol yielded diphenylurea (1·5 g.), m. p. and mixed m. p. 236°, and 5-oxo-3 : 4-diphenyl-1 : 2 : 4-oxadiazoline (0·25 g.), m. p. and mixed m. p. 167—168°.

We thank Dr. H. J. Vipond for helpful discussions and Professor A. W. Johnson for a sample of 4 : 5-dimethylphenylene-1 : 2-diamine.

THE UNIVERSITY, NOTTINGHAM. [*Received, December 4th*, 1957.]

[26] Marckwald, *Annalen*, 1895, **286**, 366.
[27] Müller, *Ber.*, 1886, **19**, 1669.

---

431. *The Conductances of Some Chlorides in Ethanol. Part I. Hydrochloric Acid, Cæsium Chloride, Magnesium Chloride, and Lanthanum Chloride.*

By A. M. EL-AGGAN, D. C. BRADLEY, and W. WARDLAW.

The conductances of very dilute solutions of hydrochloric acid, cæsium chloride, magnesium chloride, and lanthanum chloride have been measured in anhydrous ethanol at 25°. Some measurements on magnesium chloride solutions at 20° were also obtained. The effects of traces of water on the conductances of cæsium chloride and magnesium chloride were determined. Hydrochloric acid and cæsium chloride behave as strong electrolytes exhibiting ion-association in accordance with theory. The behaviour of magnesium chloride or lanthanum chloride is not unambiguously determined by conductance measurements because of the possibility of solvolysis but they are not strong electrolytes.

IN preparation for studies on the solvolysis of the chlorides of Group IV metals it was necessary to obtain molecular conductances of the chlorides of uni-, bi-, and ter-valent metals in anhydrous ethanol. For comparison with the behaviour of thorium chloride it was preferable to obtain data on chlorides of the heavier metals and to this end the

chlorides of cæsium, barium, and lanthanum were chosen. Unfortunately, the very low solubility of barium chloride precluded its measurement and magnesium chloride was studied instead. In view of the possible solvolysis of Group IV chlorides to form hydrochloric acid and the discrepancies among recorded values for the conductance of the latter we included it in this work.

Experimental

The magnitude of interionic effects with a solvent of low dielectric constant requires that measurements be made at the lowest concentrations possible. This can only be achieved under extremely rigorous conditions of purity of solvent and solutes. In particular, ethyl alcohol is very hygroscopic and although water has only a small effect on the conductivity of pure alcohol we have found that the conductivities of some electrolytes are very sensitive to water. Consequently most attention was given to producing " conductivity alcohol " and to avoiding the inclusion of water during the making up and transference of solutions.

Conductivity Alcohol.—After trial of several recorded methods for purifying alcohol an improved method was devised which readily furnished large quantities having consistently the second lowest recorded specific conductance. Absolute alcohol (5 l.) was given a preliminary azeotropic drying by fractional distillation (100 cm. column, packed with 4 mm. Fenske glass helices) with benzene (100 c.c.). After removal of the benzene, sodium (5 g., clean cut) was dissolved in the alcohol, followed by diethyl phthalate (20 c.c.), and the solution was boiled under reflux for 4 hr. The water content of the distillate was estimated by the Karl Fischer method to be *ca.* 0·002% and the specific conductivity was $3{\cdot}94 \times 10^{-9}$ mho. The only lower value reported is $1{\cdot}25 \times 10^{-9}$ mho obtained by Danner and Hildebrand [1] using a more complicated procedure in which the alcohol was finally distilled *in vacuo* into a sealed-on glass conductivity cell. In our method a large stock (4·5 l.) of conductivity alcohol was prepared and could be drawn on over a period of time during which frequent checks showed that its conductivity was unchanged. However, it was essential to purify the diethyl phthalate carefully and to pass purified nitrogen through the stillhead. Distillation of this " conductivity " alcohol from anhydrous copper sulphate or 2 : 4 : 6-trinitrobenzoic acid did not lower the specific conductivity.

Cæsium Chloride.—Commercial " pure " cæsium chloride (4·5 g.) was azeotropically dried, conductivity alcohol (100 c.c.) and benzene (80 c.c.) being used. Most of the cæsium salt appeared to remain insoluble and was separated from the final solution (70 c.c.) by decantation. The residue (4 g.) was dried *in vacuo* and analysed for chloride (gravimetrically as AgCl) and water (Karl Fischer method) (Found: Cl, 21·08; H_2O, 0·008. Calc. for CsCl: Cl, 21·05%).

Magnesium Chloride.—Hydrated magnesium chloride (5 g.; " AnalaR ") was azeotropically dried with conductivity alcohol (200 c.c.) and benzene (15 c.c.). When the clear solution had been concentrated to 100 c.c. it was allowed to cool and deposit magnesium chloride alcoholate. The crystals were separated and subjected to the foregoing treatment which was again repeated on the second crop and finally the third crop was thrice recrystallised from conductivity alcohol. The dried product was analysed for magnesium (oxine method), chloride (AgCl, gravimetric), ethoxide (method of Bradley *et al.*[2]) and water (Karl Fischer method) (Found: Mg, 6·61; Cl, 19·12; EtO, 73·42; H_2O, 0·008. Calc. for $MgCl_2,6EtOH$: Mg, 6·54; Cl, 19·08; EtO, 73·55%).

Lanthanum Chloride.—Commercial " pure " lanthanum chloride hydrate (5 g.) was azeotropically dried with conductivity alcohol (300 c.c.) and benzene (190 c.c.), and the solution evaporated to dryness since it did not crystallise. The lanthanum chloride ethyl alcoholate was then converted into the *iso*propyl alcoholate by alcohol interchange and twice recrystallised from *iso*propyl alcohol. The dried solid (6 g.) was analysed for lanthanum (precipitation as hydroxide and ignition to La_2O_3), chloride (AgCl, gravimetric), *iso*propoxide (method of Bradley *et al.*[2]) and water (Karl Fischer method) (Found: La, 32·55; Cl, 25·07; Pr^iO, 42·4; H_2O, 0·007. Calc. for $LaCl_3,3Pr^iOH$: La, 32·64; Cl, 24·99; Pr^iO, 42·4%).

Alcoholic Hydrochloric Acid.—Hydrogen chloride was generated in an all-glass apparatus by running concentrated hydrochloric acid (" AnalaR ") into concentrated sulphuric acid (" AnalaR "). The gas was passed first through concentrated sulphuric acid (" AnalaR "),

[1] Danner and Hildebrand, *J. Amer. Chem. Soc.*, 1922, **44**, 4824.
[2] Bradley, Halim, and Wardlaw, *J.*, 1950, 3450.

then through a cold-trap packed with purified glass wool at *ca.* −78°. The latter device served both to remove spray and to effect final drying. The hydrogen chloride was finally led into conductivity alcohol which was vigorously stirred (magnetically) and cooled to minimise esterification. All connections were poly(vinyl chloride) tubing. When the solution was judged to be *ca.* 0·1N the absorption of hydrogen chloride was discontinued and the solution immediately analysed and then accurately diluted with conductivity alcohol.

Potassium Chloride.—" AnalaR " reagent was crystallised four times from distilled water in Pyrex apparatus and finally from conductivity water in a platinum dish. The crystals were dried at 130° for one day, then taken to dull red heat, transferred to an agate mortar, and ground. The powder was dried for 2 days at 180° and allowed to cool in the presence of phosphoric oxide. Qualitative tests showed no magnesium, sodium, or sulphate and the product gave a neutral solution.

Benzoic Acid.—Benzoic acid (" AnalaR ") was crystallised thrice from hot conductivity water then dried at 110°. It melted at 121·7°.

Nitrogen.—Since nitrogen was continuously passed through the refluxing conductivity alcohol it was essential that the gas be highly purified. After considerable research the following

FIG. 1.

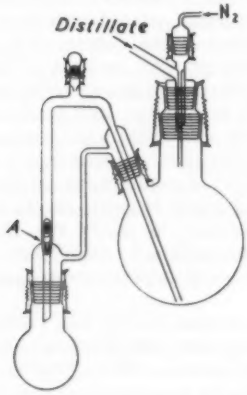
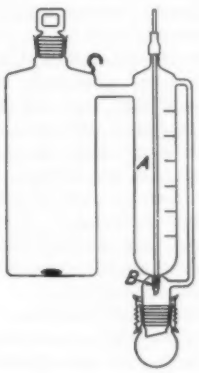


FIG. 2.



procedure was judged to be most efficient. Commercial " oxygen-free " nitrogen was passed through (*a*) a cotton-wool dust-trap, (*b*) a tube of soda-lime to remove carbon dioxide, (*c*) a Kraus and Parker [3] scrubber containing dilute potassium hydroxide solution, (*d*) a spray trap, (*e*) a second scrubber containing dilute phosphoric acid to remove ammonia, (*f*) another spray trap, (*g*) a wash-bottle containing concentrated sulphuric acid for preliminary drying, (*h*) a spray trap containing a glass-wool filter, (*i*) a column of silica gel, (*j*) a column packed with phosphoric oxide suspended on glass-wool, and finally another glass-wool filter. Connections were made as before. Nitrogen purified in this manner was used exclusively in all operations.

Conductivity Still.—The fractionating column described above was fitted to a total-condensation variable-take-off still-head in which the reflux ratio was controlled by the inclination of a crescent-shaped glass rod placed beneath the returning condensate. This device was externally operated by a glass lever acting through a standard ground-glass joint arranged so that the conductivity alcohol did not pass through taps or joints on leaving the still-head. The collected condensate passed through a dripper on to another crescent-shaped divider which allowed the alcohol to pass into either a built-in conductivity cell or the storage flask (2 l.) shown in Fig. 1. The conductivity cell (capacity 40 c.c.) was of the siphon type and contained a thermometer well and it allowed frequent checks on the specific conductivity of the alcohol. The alcohol was siphoned as required from the storage vessel through a magnetically operated ground-glass valve (*A* in Fig. 1) directly into the other conductivity cell, a counter-current of nitrogen excluding air during the attachment or detachment of the cell.

[3] Kraus and Parker, *J. Amer. Chem. Soc.*, 1922, **44**, 2429.

Conductivity Cell.—The cell was of approx. 750 c.c. capacity and was constructed in Pyrex glass. The dipping electrodes were of bright platinum with an area approx. 7 cm.^{2} and separated by about 7 mm. The electrodes were welded to strips of thin platinum foil which made contact *via* pinched glass seals to the mercury wells. The electrode assembly was held rigidly by glass pillars. Solution in the cell could be magnetically stirred.

Preparation of Solution.—A relatively concentrated solution was made up in a weight burette (Fig. 2) by weighing in a sample of solute, then collecting pure solvent, and using a magnetic stirrer to speed dissolution. The burette could be weighed to determine the total weight of solution. The solution was transferred to the roughly graduated limb *A* by tilting and then dispensed through the ground glass valve *B* into the main conductivity cell. The conductance of the concentrated solution was also measured directly in a small cell and its purity and stability could thus be frequently checked. Instead of using the Ostwald–Arrhenius dilution procedure we adopted Whetham's method.[4] First the cell was filled with a known weight of pure solvent (approx. 450 c.c.) and its conductance was measured. Then small successive additions of concentrated solution were made from the weight burette, and the conductance was remeasured. In this manner the errors due to contamination of the solution, which must accumulate during a dilution procedure, are made least in the most dilute solutions. The advantage of the Ostwald–Arrhenius method is the elimination of errors due to adsorption but experiments in which powdered glass was added to dilute solutions showed that adsorption errors were negligible in our work whereas the sensitivity of the solvent to contamination was very high.

Determination of the Cell Constant.—The cell constant was determined by measuring the conductance of freshly prepared potassium chloride solutions using Davies's data. The following values for the cell constant obtained at approximately 8-monthly intervals reflect the stability of the cell: 0·078849, 0·078853, and 0·078842. These determinations were confirmed by the method recommended by Ives and Sames [6] using benzoic acid solutions.

Density Determinations.—Measurements on alcohol and some of the more concentrated electrolyte solutions were made at various temperatures, by using an all-glass dilatometer containing two vertical " Veridia " capillaries (2·0 mm. bore) as described previously.[7] The value for pure alcohol at 25·00° was d_4^{25} 0·78479 (lit.,[8] 0·78506).

Cleaning Procedure.—Experiments showed that repeated treatment of the conductivity cell with chromic acid cleaning mixtures gave erratic results and the following method was adopted instead. The apparatus was cleaned with chromic–nitric acid mixture, then rinsed with distilled water, and subjected to prolonged steaming. In the latter stage we found that steam generated from alkaline potassium permanganate solution was unsuitable (cf. Ives *et al.*[9]) and conductivity water was used instead. After steaming, the apparatus was dried at 140° for several hours and allowed to cool in a stream of nitrogen. After this initial treatment the apparatus was no longer treated with chromic acid and at the end of each experiment it was rinsed thoroughly with conductivity water, steamed, and dried. This procedure was applied to all apparatus and gave reproducible results.

Electrical Measurements.—A Doran conductivity bridge was suitably adapted for this work and the usual precautions required for a.c. measurements were observed. For determining the specific resistance of the alcohol and of dilute solutions the " shunt " method was used. An 80,000 ohm Sullivan non-inductive resistance was first measured alone and then with the conductivity cell in parallel. The cell was kept at 25° ± 0·01° in a thermostat, the temperature being checked with a standard thermometer. Weights were corrected for buoyancy when necessary. The solvent conductance was subtracted from the conductance of the solution and this correction did not exceed 1—2% for the most dilute solutions.

Results and Discussion

Hydrochloric Acid.—The results are given in Table 1 in which C is the concentration in equivs./l. and Λ_c is the corresponding equivalent conductance. The results conformed

[4] Whetham, *Phil. Trans.*, 1900, **194**, 321.
[5] Davies, *J.*, 1937, 434.
[6] Ives and Sames, *J.*, 1943, 512.
[7] Bradley, Kay, and Wardlaw, *J.*, 1956, 4916.
[8] International Critical Tables.
[9] Ives and Riley, *J.*, 1931, 1999; Feates, Ives, and Pryor, *J. Electrochem. Soc.*, 1956, **103**, 580.

to the equation $\Lambda_c = 83{\cdot}60 - 395\sqrt{C}$ as is shown by the calculated values. The Kohlrausch slope is practically double the theoretical value (199·6) calculated from the Onsager

TABLE 1. *Hydrochloric acid in ethanol.*

10^4C	Λ_c	$83{\cdot}60-395\sqrt{C}$	10^3K	10^4C	Λ_c	$83{\cdot}60-395\sqrt{C}$	10^3K
0·9120	79·80	79·83	8·36	8·311	72·22	72·21	8·25
1·3805	78·99	78·96	7·99	13·995	68·87	68·82	8·37
3·4351	76·28	76·28	7·83	18·320	66·81	66·70	8·39
4·556	75·16	75·17	7·84				

equation and ion-association evidently occurs. The method of Fuoss [10] was used to determine the thermodynamic dissociation constant K. The mean ionic activity coefficient $f_\pm$ was determined from the Debye–Hückel equation which for ethanol at 25° takes the form

$$-\log f_\pm^2 = (5{\cdot}954\sqrt{\alpha C})/(1 + 0{\cdot}5921a_i\sqrt{\alpha C})$$

where α is the degree of dissociation of ion-pairs and a_i is the average effective diameter (Å) of the ions. However, trial computations showed that best agreement was obtained by ignoring a_i and using the simplified equation $-\log f_\pm^2 = 5{\cdot}954\sqrt{\alpha C}$. The limiting equivalent conductance and the dissociation constant were then found to be $\Lambda_0 = 82{\cdot}46$ and $K = 8{\cdot}23 \times 10^{-3}$. K is extremely sensitive to error as shown in the calculated values of K in Table 1. Λ_0 is significantly lower than the value (83·60) obtained by extrapolation of the Kohlrausch equation. Other values have been reported for Λ_0, *viz.*, 81·8 (ref. 12), 83·8 (ref. 13), and 84·25 (ref. 14). In particular the work of Bezman and Verhoek [14] showed that the conductance of ethanolic hydrochloric acid is sensitive to water and, in the region $[H_2O] = 0$—1·4M, Λ_0 decreases with increase in water content. Our value for Λ_0 corresponds to the feasible water content of 0·0025% according to their results, although their conductivity alcohol was less pure than ours.

Cæsium Chloride.—The data for cæsium chloride are given in Table 2 and represent three completely independent runs arranged in order of ascending concentration irrespective of the number of the run. The conductances conform to the equation:

$$\Lambda_c = 48{\cdot}55 - 268{\cdot}9\sqrt{C}$$

as shown in Table 2.

TABLE 2. *Cæsium chloride in ethanol.*

10^4C	Λ_c	$\Lambda_{calc.}$	10^3K	10^4C	Λ_c	$\Lambda_{calc.}$	10^3K	10^4C	Λ_c	$\Lambda_{calc.}$	10^3K
0·9698	45·85	45·91	6·0	1·396	45·34	45·24	6·0	1·742	44·95	45·00	6·1
0·9803	45·93	45·89	6·8	1·497	45·26	45·26	6·0	1·823	44·94	44·94	6·6
1·0145	45·85	45·84	6·5	1·506	45·30	45·25	6·7	1·837	45·00	44·90	7·1
1·0857	45·79	45·75	6·8	1·577	45·19	45·17	6·5	1·975	44·86	44·77	7·1
1·1109	45·75	45·72	6·6	1·607	45·11	45·14	6·2	1·997	44·77	44·76	6·6
1·179	45·67	45·67	6·7	1·654	45·13	45·12	6·7	2·198	44·56	44·57	6·6
1·341	45·50	45·47	6·9	1·712	45·07	45·03	6·6				

The abnormally high Kohlrausch slope (theory 152·4) suggested the occurrence of ion-association and this was confirmed by application of Fuoss's method which gave $\Lambda_0 = 48{\cdot}01$ and $K = 6{\cdot}61 \times 10^{-3}$. The complete Debye–Hückel expression for the activity coefficient was used for several values of a_i and any value between 5·0—8·0 Å gave satisfactory calculations. The individual values of K in Table 2 were based on $a_i = 5{\cdot}0$ Å. In the Bjerrum theory [11] for ion-association the dissociation constant K may be calculated as a

[10] Fuoss, *J. Amer. Chem. Soc.*, 1935, **57**, 488.
[11] Bjerrum, *Kgl. danske Videnskab. Selskab*, 1926, **7**, 9.
[12] Goldschmidt and Dahl, *Z. phys. Chem.*, 1925, *A*, **114**, 1.
[13] Murray-Rust and Hartley, *Proc. Roy. Soc.*, 1929, *A*, **126**, 84.
[14] Bezman and Verhoek, *J. Amer. Chem. Soc.*, 1945, **67**, 1330.

XUM

function of the distance of closest approach a of the ions. It is interesting that a value of $a = 3{\cdot}46$ Å, the sum of the *unsolvated* ionic radii,[15] would require a value of K of the right order. Addition of water to alcoholic cæsium chloride caused a decrease in conductance as shown by the data in Table 3 in which the initial concentration of cæsium

TABLE 3.

Water (%)	0	0·022	0·056	0·183	0·286	0·465	0·700	0·948
$10^6\kappa$ (mhos)	4·662	4·650	4·642	4·631	4·627	4·618	4·607	4·596

chloride was 10^{-4} mole/l. This behaviour can be ascribed mainly to the increase in viscosity caused by the addition of water. For example, a 0·1% aqueous alcohol solution has a viscosity 0·3% higher than pure alcohol whilst the cæsium chloride solution with 0·1% of water has a conductance *ca.* 0·5% lower than that of the anhydrous solution.

Magnesium Chloride.—In view of the ion-association found with the uni-univalent electrolytes the measurements on magnesium chloride were taken to extremely low concentrations. Preliminary Kohlrausch plots, based on complete ionisation of magnesium chloride as a bi-univalent electrolyte ($\frac{1}{2}MgCl_2 \longrightarrow \frac{1}{2}Mg^{2+} + Cl^-$), suggested that dissociation was incomplete whilst an Ostwald plot ($c\Lambda_c$ *versus* $1/\Lambda_c$, where c = normality and Λ_c = equivalent conductance) was linear. The data are presented in Table 4 in which the values of $\Lambda_{calc.}$ were obtained at each concentration by using the values of the apparent limiting equivalent conductance ($\Lambda'_0 = 38{\cdot}98$) and the " dissociation constant " ($K_c = 1{\cdot}876 \times 10^{-4}$) obtained by application of the least-squares method to the Ostwald plot.

TABLE 4.

10^5C	Λ_c	$\Lambda_{calc.}$	10^5C	Λ_c	$\Lambda_{calc.}$	10^5C	Λ_c	$\Lambda_{calc.}$
1·0420	36·98	36·84	2·9725	34·09	34·25	5·2348	31·63	31·73
1·4435	36·42	36·28	3·5129	33·78	33·56	5·9446	31·00	31·12
1·5218	36·27	36·20	3·5436	33·49	33·49	5·9952	31·04	31·07
1·9244	35·44	35·62	4·0911	33·05	32·92	6·7512	30·48	30·45
2·0634	35·54	35·43	4·3566	32·67	32·61	6·7541	30·35	30·45
2·4690	34·75	34·85	4·6014	32·56	32·41	7·5279	29·76	29·82
2·4910	34·98	34·82	5·2094	31·94	31·77	7·6414	29·77	29·73
2·9334	34·14	34·27						

These results involve two separate runs and are given in ascending order of concentration irrespective of the run. Although the Ostwald relation obviously applied very well to the results this must be fortuitous because on the one hand interionic effects are ignored whilst on the other the proposed ionisation would require a linear plot of $(c\Lambda_c)^2$ against $1/\Lambda_c$. Alternatively, if the magnesium chloride functions as a weak uni-univalent electrolyte (*viz.*, $MgCl_2 \rightleftharpoons MgCl^+ + Cl^-$) then the limiting equivalent conductance deduced from the Ostwald plot (using molar concentration of $MgCl_2$ instead of equivalent concentration) would be 77·96 which is impossibly high (cf. Λ_0 for hydrochloric acid = 82·46). Whilst our work was in progress Dawson and Golben [16] reported their results for the conductances of magnesium halides in alcohol at 20°. They showed that the variation of conductance with concentration was consistent with the magnesium chloride's behaving as a strong electrolyte in its first ionisation (*i.e.*, $MgCl_2 \longrightarrow MgCl^+ + Cl^-$) and as a weak electrolyte in the secondary ionisation (*i.e.*, $MgCl^+ \rightleftharpoons Mg^{2+} + Cl^-$). Moreover, they applied the appropriate corrections for interionic effects and used activities instead of concentrations although some assumptions were made. Thus it was assumed that the activity coefficients for the univalent ions MgX^+ and Cl^- were equal over the concentration

[15] Sidgwick, " The Chemical Elements and Their Compounds," Oxford Univ. Press, 1950, Vol. I, p. xxix.
[16] Dawson and Golben, *J. Amer. Chem. Soc.*, 1952, **74**, 4134.

XUM

range studied and it is not clear how they deduced the limiting equivalent conductance for MgX^+. Moreover, they pointed out that the activity coefficient for magnesium ions was one of the two decisive factors in their computation but in order to deduce this coefficient from the Debye–Hückel equation it was necessary to estimate the " minimum distance of approach " for solvated magnesium ions (a_i) and this may well be an important source of error (*e.g.*, omission of the term involving (a_i) would incur an error of *ca.* 0·4% in $-\log f_i$ at a normality of 10^{-6} but about 4% at a normality of 10^{-4}). It is also noteworthy that these authors showed that a simple mass-law plot using concentrations instead of activities and ignoring interionic effects gave the required linear relation and a value of Λ_0 (41·08) close to that obtained (41·75) by the refined method. In addition, they obtained a value of 40·64 by using an Ostwald plot (assuming a uni-univalent ionisation with normality as concentration) and 39·57 from a plot of $(C\Lambda)^2$ against $1/\Lambda$ (*i.e.*, applications of mass law to simultaneous binary dissociation $MgCl_2 \rightleftharpoons Mg^{2+} + Cl^-$) although in the latter the linearity of the plot was less extensive than for the former. In view of these computations we feel that there is some ambiguity concerning the ionisation of magnesium chloride in ethanol and that there is a possibility of solvolysis occurring {*i.e.*, either (1) $MgCl_2 + EtOH \rightleftharpoons MgCl(OEt) + H^+ + Cl^-$, or (2*a*) $MgCl_2 \longrightarrow MgCl^+ + Cl^-$, or (2*b*) $MgCl^+ + EtOH \rightleftharpoons MgCl(OEt) + H^+ + Cl^-$}. It is clear that irrespective of the precise relation between conductance and concentration the value of the molar conductance extrapolated to infinite dilution would in these cases approximate to the limiting equivalent conductance for hydrochloric acid. We have already mentioned that the limiting molar conductance obtained by using the Ostwald plot on our results was close to the limiting equivalent conductance for hydrochloric acid. It is evident that the problem will only be resolved by carrying out some independent experiments such as the measurement of hydrogen-ion concentrations and the examination of solutions of magnesium chloride ethoxide. Before leaving magnesium chloride we report some results for the conductance at 20°. These experiments were carried out as a check on Dawson and Golben's data since their values for Λ at 20° seemed high compared with ours at 25°. Our results for 20° (Table 5) are considerably lower than Dawson and Golben's. It is

TABLE 5.

10^4C_M	4·859	7·210	10·044	14·252	18·637	23·317	28·592	36·639
Λ_M	68·69	66·22	63·685	61·55	58·73	56·27	54·03	51·80

possible that the discrepancy is due to our solutions' having a lower water content than theirs because the conductance of ethanolic magnesium chloride is very sensitive to traces of water, as shown in Table 6 (the concentration of magnesium chloride was $2·5 \times 10^{-4}$ equiv./l.). It is clear that even a low concentration of water causes a marked increase in conductance (cf. with the decrease for strong electrolytes) and emphasizes the difficulties in obtaining accurate results at low concentration in this solvent.

TABLE 6.

Water (%)	0	0·083	0·207	0·285	0·317	0·411	0·518
$10^4\kappa$	5·376	5·857	6·133	6·323	6·401	6·531	6·665

Lanthanum Chloride.—The variation of conductance with concentration of lanthanum chloride showed typical weak electrolytic behaviour. A plot of $\Lambda_M C_M$ against $1/\Lambda_M$ took the form of two intersecting straight lines. In the most dilute region extrapolation of the line to infinite dilution gave $(\Lambda'_0)_1 = 70·57$ and $(K_c)_1 = 2·468 \times 10^{-5}$. The results in this region are given in Table 7 and represent three separate runs arranged in order of ascending concentration irrespective of the number of the run. The results for concentrations above $2·8 \times 10^{-5}$ mole/l. fall on another straight line which gave on extrapolation

XUM

to infinite dilutions: $(\Lambda'_0)_2 = 50{\cdot}55$; $(K_c)_2 = 1{\cdot}293 \times 10^{-4}$. The data for this region are given in Table 8. The two values of $\Lambda_{calc.}$ in parentheses were calculated from the equation of the first straight line and although these two points are the nearest to that line it is evident that they are not on it.

TABLE 7.

10^4C_M	Λ_M	$\Lambda_{calc.}$	10^4C_M	Λ_M	$\Lambda_{calc.}$	10^4C_M	Λ_M	$\Lambda_{calc.}$
6·524	58·01	58·06	11·479	52·20	52·42	15·503	49·08	49·10
6·571	57·59	57·96	11·853	51·89	52·10	18·132	47·40	47·29
8·383	55·97	55·67	12·485	51·47	51·53	18·575	47·12	47·00
8·478	55·80	55·55	15·049	49·78	49·46	19·101	46·23	46·66
8·582	55·59	55·44	15·382	48·70	49·20	20·850	45·95	45·65
9·790	53·56	54·10						

TABLE 8.

10^5C_M	Λ_M	$\Lambda_{calc.}$	10^5C_M	Λ_M	$\Lambda_{calc.}$
2·8405	42·75	42·65 (41·91)	3·7721	40·97	40·90
2·8965	42·47	42·55 (41·68)	4·0161	40·25	40·46
2·9190	42·41	42·48	4·1250	40·33	40·30
3·2489	41·99	41·86	4·1836	40·24	40·21
3·3289	41·69	41·69	4·6239	39·90	39·48
3·4168	41·42	41·56	4·6965	39·20	39·43
3·6350	41·21	41·15	4·7129	39·32	39·37

Let us consider first the value of 70·57 for the limiting molecular conductance of lanthanum chloride. Obviously the possibility of complete ionisation (*viz.*, $LaCl_3 \longrightarrow La^{3+} + 3Cl^-$) may be ruled out because the chloride ions alone would contribute 72·9 (if Barak and Hartley's value[17] of 24·3 is accepted for the equivalent conductance of the chloride ion), making the conductance of the La^{3+} ion $-2{\cdot}6$. It is very interesting that at such a low concentration the lanthanum chloride does not appear to behave as a ter-univalent electrolyte. In view of the difficulties encountered in interpreting the conductance data for magnesium chloride it is not profitable to theorise deeply on those for lanthanum chloride. However, the existence of two intersecting straight lines in the Ostwald plot is noteworthy and puzzling. Thus the straight line covering the higher concentration range gave an apparent limiting molecular conductance of 50·55 which suggests the presence of a weak uni-univalent electrolyte (cf. CsCl 48·01) and might correspond to the first stage of ionisation as follows: $LaCl_3 \rightleftharpoons LaCl_2^+ + Cl^-$. The second straight line, which gave a limiting molecular conductance of 70·57 (cf. $MgCl_2$ 77·96), presumably corresponds to the secondary ionisation: $LaCl_2^+ \rightleftharpoons LaCl^{2+} + Cl^-$.

It is clear that more work on the electrochemistry of ethanolic solutions is needed before the electrolytic behaviour of these salts can be understood. In particular the determination of transport numbers and activity coefficients would be invaluable.

One of us (A. M. A.) thanks the Egyptian Government for a Grant and Alexandria University for study-leave. We are indebted to Dr. D. J. G. Ives for his valuable advice and for a supply of conductivity water.

BIRKBECK COLLEGE, MALET STREET, LONDON, W.C.1. [*Received, November 4th*, 1957.]

[17] Barak and Hartley, *Z. physikal. Chem.*, 1933, **165**, 273.

432. *Solubility and Heat of Solution of 2 : 4 : 6-Trinitrotoluene in Sulphuric Acid at 25°.*

By B. J. Kirkbride and P. A. H. Wyatt.

The solubility of 2 : 4 : 6-trinitrotoluene in sulphuric acid at 25° in the presence of disulphuric acid, water, or potassium hydrogen sulphate up to concentrations of about 0·4m was measured. It is increased by addition of disulphuric acid and decreased by addition of water; in the latter case irregularities appear near 0·2m-H_2O,HSO_4 similar to those observed in cryoscopy. Potassium hydrogen sulphate increases the ratio of trinitrotoluene to sulphuric acid in the solution but hardly affects the mole fraction of the nitro-compound. The heat of infinite dilution of a saturated solution of trinitrotoluene is less than 100 cal. mole^{-1}, and the heat of solution of the solid, 4·6 kcal. mole^{-1}, is close to the heat of fusion. These observations help in a discussion of the magnitude of the solubility of this compound in sulphuric acid, which is 13·15 g. per 100 g. of H_2SO_4 at 25°.

Electrolytes exert specific influences upon the cryoscopic behaviour of polynitro-compounds in the solvent sulphuric acid and an explanation in terms of "salting-out" and "salting-in" was suggested,[1] to test which we have investigated the solubility of 2 : 4 : 6-trinitrotoluene in sulphuric acid with and without the addition of other electrolytes. Heats of dilution and solution of this solute were also determined to obtain a broader picture of the nature of solutions of non-electrolytes in this solvent.

Experimental

All materials were prepared or purified as described by Brayford and Wyatt.[1]

Solubilities.—The solubility was measured of trinitrotoluene in pure sulphuric acid and in sulphuric acid containing hydroxonium hydrogen sulphate (*i.e.*, in aqueous acid), disulphuric acid, or potassium hydrogen sulphate as third component. Since freezing-point measurements were used to prepare the sulphuric acid solutions, it was convenient to carry out the equilibration with solid trinitrotoluene in a cryoscope.. A sample (about 120 g.) of sulphuric acid containing the third component was first prepared therein, and an excess of solid trinitrotoluene then added. The thermometer (a 10-junction copper–constantan thermocouple) was replaced by a glass stopper, and the cryoscope was allowed to equilibrate for 40—80 hr. at 25·1°, the contents being continuously stirred. Samples were then taken with the simple filter and suction device shown in Fig. 1. Each sample was delivered directly into a weighed weighing bottle and analysed for trinitrotoluene by the titanous sulphate–ferric alum procedure.[2,3,4] (Alcohol was used in the dilution of the samples to keep the trinitrotoluene in solution.) Pure 2 : 4 : 6-trinitrotoluene was used to standardize the titanous sulphate solution.

Heats of Solution.—The apparatus for thermal measurements has been described.[5] With pure sulphuric acid in the calorimeter, the heat changes were measured as successive amounts of trinitrotoluene were added, both as a *ca.* 0·5m-solution in sulphuric acid and as a solid.

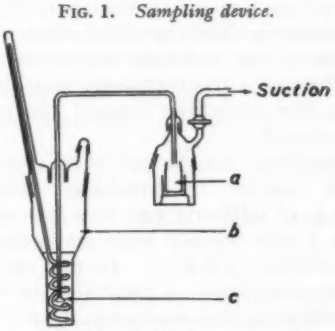
Results.—In Fig. 2 the results of the solubility measurements are shown in terms of the number of moles of trinitrotoluene dissolved per 1000 g. of sulphuric acid. Determinations were reproducible to about 0·5%. When converting the results into mole fractions for Table 1, allowance was made for the ionization of potassium and hydroxonium hydrogen sulphates into two particles, but disulphuric acid was treated as a non-electrolyte—its partial ionization[6] would not affect the calculated value for the mole fraction of trinitrotoluene, provided that no attempt was made to allow for ionic solvation, since the ionization involves no change in the

[1] Brayford and Wyatt, *J.*, 1955, 3453.
[2] Knecht and Hibbert, "New Methods of Volumetric Analysis," Longmans Green, London, 1918.
[3] Callan and Henderson, *J. Soc. Chem. Ind.*, 1922, **41**, 157T.
[4] Hammett and Chapman, *J. Amer. Chem. Soc.*, 1934, **56**, 1282.
[5] Kirkbride and Wyatt, *Trans. Faraday Soc.*, 1958, **54**, 483.
[6] Gillespie, *J.*, 1950, 2493.

number of particles: $H_2S_2O_7 + H_2SO_4 \rightleftharpoons H_2SO_4^+ + HS_2O_7^-$. Similarly, the self-dissociation of the solvent does not affect the solute mole fraction.

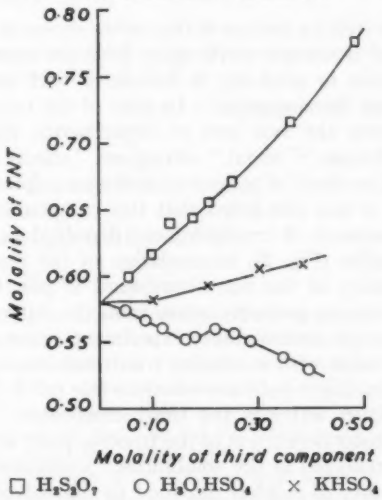
Table 2 contains the thermal results. The small heat changes observed when trinitrotoluene is added in solution are just greater than the probable error (estimated [5] as 50 cal. mole^{-1}). The experimental error was probably rather larger when the solid was added, however, since it was difficult to correct [5] for the difference between the temperatures of the solid and the calorimeter contents before the addition was made. Experience with the addition of

FIG. 1. *Sampling device.*



a, Weighing bottle in wire cradle; *b*, cryoscope; *c*, No. 2 sintered filter disc.

FIG. 2. *Solubility of* 2 : 4 : 6-*trinitrotoluene in sulphuric acid solutions at* 25°.



liquids under the same conditions showed that this difference seldom exceeded 2°, but a correction based on this figure would imply that the values recorded for the heat of solution (Table 2) could be 150 cal. mole^{-1} low. An error of this magnitude does not affect the subsequent discussion.

TABLE 1. *Composition (mole fractions) of saturated trinitrotoluene solutions at* 25°.

(*a*) Water as third component			(*b*) $H_2S_2O_7$ as third component			(*c*) $KHSO_4$ as third component.		
T.N.T.	$H_3O^+ + HSO_4^-$	H_2SO_4	T.N.T.	$H_2S_2O_7$	H_2SO_4	T.N.T.	$K^+ + HSO_4^-$	H_2SO_4
0·0537	0·000	0·9463	0·0553	0·00525	0·9395	0·0530	0·01813	0·9289
0·0529	0·00884	0·9383	0·0564	0·00905	0·9346	0 0529	0 03644	0 9107
0·0519	0 01422	0 9339	0·0583	0·01204	0·9297	0·0532	0·05296	0·8938
0·0509	0·02170	0·9274	0·0585	0·01593	0·9256	0·0526	0·06648	0·8809
0·0500	0·02878	0·9212	0·0592	0·01872	0·9221			
0·0498	0·03243	0·9178	0·0603	0·02247	0·9172			
0·0501	0·03841	0·9115	0·0635	0·03231	0·9042			
0·0494	0·04470	0·9059	0·0678	0·04187	0·8903			
0·0488	0·04939	0·9018						
0·0471	0·06023	0·8927						
0·0460	0·06842	0·8856						

The presence of trinitrotoluene seems to produce very little change in the specific heat of sulphuric acid. At molalities of 0·0055, 0·0111, 0·0165, 0·0266, and 0·0318 values of $0·337_7$, $0·338_4$, $0·337_2$, $0·337_5$, and $0·336_9$ cal. deg.$^{-1}$ g.$^{-1}$ respectively were recorded (cf. the corresponding value of 0·3373 cal. deg.$^{-1}$ g.$^{-1}$ for the pure solvent [5]).

TABLE 2.

(*a*) Relative partial molar heat content of trinitrotoluene in sulphuric acid solutions at 25°.
Trinitrotoluene added as a 0·4989m solution.

Mean molality	0·00277	0·00832	0·01382	0·01922
$\overline{H}_2$ relative to 0·5m (cal. mole^{-1})	83	76	0	68

(*b*) Heat of solution of crystalline trinitrotoluene in sulphuric acid at 25°.

Mean molality	0·02272	0·02923
$\overline{H}_2$ relative to pure crystals (cal. mole^{-1})	4574	4535

DISCUSSION

A striking feature of the curves shown in Fig. 2 is their similarity to the curves obtained in the cryoscopic work, apart from the expected change in direction of the effects; *i.e.*, a decrease in solubility is associated with an increase in the molecular depression of the solvent freezing-point. In spite of the tenfold difference in trinitrotoluene concentration between the two sets of experiments, therefore, the solubilities support the general conclusions [1,7] about " salting-out " effects in this solvent.

The effects of potassium hydrogen sulphate are puzzling. On the basis of the cryoscopic data it was concluded that this compound should " salt-in " trinitrotoluene. Although the amount of trinitrotoluene dissolved per 1000 g. of sulphuric acid does increase appreciably (Fig. 2), recalculation of the results on a mole-fraction basis shows that the solubility of the nitro-compound is practically constant (Table 1). In this case, the discrepancy probably arises from the difference in concentration of trinitrotoluene in the cryoscopic and solubility experiments, since some indication of an increase in the molecular depression with increasing trinitrotoluene concentration was actually observed in potassium hydrogen sulphate solutions [see ref. 1, Table 3 (*d*)].

When water is the third component, the irregularities recorded previously in the molecular depression of the freezing-point of the solvent in the neighbourhood of 0·2m are also reflected in the solubilities. Comparison with the similar effects of water upon the solubility of sulphur dioxide [8] in this solvent, and upon the density, leads us to suppose that the causes for the changes in non-electrolyte activity coefficients reside in modifications in the structure and constitution of the solvent itself rather than in any specific chemical involvement of the non-electrolyte (chemical solvation).

The magnitude of the solubility in the pure solvent (mole fraction 0·0537) can be interpreted from thermal data. The very small heat absorption upon dilution of a 0·5m solution shows that the heat of infinite dilution of a saturated solution must be negligible (less than 100 cal. mole^{-1}). It is also significant that the heat of solution of the solid is very similar to the heat of fusion of trinitrotoluene. Unfortunately there is no record of a direct determination of the heat of fusion, but the values obtained from melting curves [9-12] of trinitrotoluene in mixtures with compounds of similar structure have usually been quoted as 4·6 or 4·9 kcal. mole^{-1}. This again provides evidence that the non-electrolyte probably exists in solution as simple molecules and not in chemically solvated form.

Although the absence of marked thermal changes indicates that departures from ideality in these solutions are mainly due to entropy effects, the standard theory of athermal solutions is not in itself sufficient to account for all the properties because it accounts for *negative* deviations from Raoult's law,[13] *i.e.*, for a solubility greater than the ideal value

[7] Wyatt, *J.*, 1954, 2647.
[8] Miles and Carson, *J.*, 1946, 786.
[9] Auwers, *Z. phys. Chem.*, 1899, **30**, 300.
[10] Pastak, *Bull. Soc. chim. France*, 1926, **39**, 82.
[11] Timmermans, *Bull. Soc. chim. Belg.*, 1935, **44**, 17.
[12] Rinkenbach and Hall, *J. Amer. Chem. Soc.*, 1924, **46**, 2637.
[13] Hildebrand and Scott, " The Solubility of Non-electrolytes," Reinhold, New York, 3rd edn., Chap. 6.

(and effects in the same direction would also be required by a chemical solvation treatment). A heat of fusion [12] of 4·6 kcal. mole^{-1} and m. p. 80·5° would require an ideal solubility at 25° of 0·30 in mole-fraction terms. Thus we have a considerable *positive* deviation from Raoult's law. Qualitatively the reduced solubility can be accounted for by supposing that sulphuric acid behaves as an " associated " solvent towards non-electrolytes of lower polarity. In view of the small changes of heat content, the positive excess free energy of solution must be associated with a negative excess entropy, as is the case for non-electrolytes in water; and theories of this loss of entropy on solution could obviously be applied to both solvents. For example, according to Frank and Evans,[14] the non-electrolyte would be pictured as inducing a greater " crystallinity " of sulphuric acid in its vicinity.

We thank Dr. T. M. Walters for the trinitrotoluene, and the Department of Scientific and Industrial Research for the award of a maintenance grant (to B. J. K.).

SHEFFIELD UNIVERSITY. [*Received, January 13th*, 1958.]

[14] Frank and Evans, *J. Chem. Phys.*, 1945, **13**, 507.

---

433. *The System* $CaO–Al_2O_3–H_2O$ *at* 5°.

By F. G. BUTTLER and H. F. W. TAYLOR.

The solubility relations in this system at 5° have been studied by experiments in which lime was added to supersaturated calcium aluminate solutions, and also in which hydrated alumina, cubic hydrated tricalcium aluminate ($3CaO,Al_2O_3,6H_2O$), or hydrated monocalcium aluminate ($CaO,Al_2O_3,10H_2O$) was added to water or lime solutions. Stable or metastable solubility curves were determined for each of these compounds, and also for the hexagonal or pseudohexagonal hydrated calcium aluminates $2CaO,Al_2O_3,8H_2O$ and $4CaO,Al_2O_3,19H_2O$. The approach to equilibrium was studied as well as the stable or metastable equilibrium states. The results differ from those reported at 21° or above, notably in the reduced rate of change of the other hydrated calcium aluminates into the cubic one, and in the existence of a well-defined metastable solubility curve for hydrated monocalcium aluminate. This compound has a virtually stable field of existence in the system at 5°, provided that equilibrium with well-crystallised gibbsite is not attained.

STUDIES on the system $CaO–Al_2O_3–H_2O$ have great practical value as they throw light on the setting of high-alumina and Portland cements. Previous work on the phase equilibria at room temperatures and above was reviewed by Steinour,[1] and the system has since been studied by d'Ans and Eick [2] at 20°, Peppler and Wells [3] at 50—250°, and Majumdar and Roy [4] at 100—1000°. When high-alumina cement pastes with CaO,Al_2O_3 as the main constituent set at room temperature, the main product is a hydrated monocalcium aluminate, $CaO,Al_2O_3,10H_2O$. This compound was first described by Assarsson,[5] who found that it was relatively persistent in aqueous suspensions at low temperatures, but not in those at room temperature. The present study was made to determine the solubility curves for the various compounds at 5°, and the stability of $CaO,Al_2O_3,10H_2O$ relative to the others.

[1] Steinour, " Aqueous Cementitious Systems containing Lime and Alumina," Bull. 34 of the Portland Cement Association, Chicago, 1951.
[2] d'Ans and Eick, *Zement-Kalk-Gips*, 1953, **6**, 197.
[3] Peppler and Wells, *J. Res. Nat. Bur. Stand.*, 1954, **52**, 75.
[4] Majumdar and Roy, *J. Amer. Ceram. Soc.*, 1956, **39**, 434.
[5] Assarsson, *Sver. Geol. Undersökn. Ansbok.*, 1933, **27**, 22; 1936, **30**, 1; *Zement*, 1934, **23**, 1, **15**; *Z. anorg. Chem.*, 1935, **222**, 321.

Experimental

Materials.—Calcium oxide was made by igniting " AnalaR " calcium carbonate and was used only when fresh. Hydrated alumina was made from pure aluminium turnings. These were degreased with ether, etched with aqueous sodium hydroxide, washed thoroughly, and placed for a few seconds in very dilute mercuric chloride solution. They were again washed and then left in a large volume of water until hydrated alumina had been formed. The solid was filtered off and washed with acetone, which was removed in a current of air. The Al_2O_3 content (60·08%) corresponded approximately to the composition $Al(OH)_3$; *X*-ray photographs of the product showed it to be quite well-crystallised bayerite. $CaO,Al_2O_3,10H_2O$ was made by hydrating finely ground pure CaO,Al_2O_3 (20 g.) with boiled distilled water (2 l.) at 5°. The solid was filtered off and dried in two lots (X and Y) (anhydrous $CaCl_2$). Carbon dioxide-free conditions were maintained throughout. Analyses gave for X: CaO, 20·0; Al_2O_3, 38·3; H_2O, 41·8%, and for Y, CaO, 18·4; Al_2O_3, 35·2; H_2O, 46·4%. The water contents were less than for $CaO,Al_2O_3,10H_2O$ (53·3%), which is thus only a nominal formula. The only solid phase detected by *X*-rays was $CaO,Al_2O_3,10H_2O$, though a little alumina must have been present as the molar ratio $CaO : Al_2O_3$ was 0·95. Cubic hydrated tricalcium aluminate, $3CaO,Al_2O_3,6H_2O$, was a pure specimen kindly supplied by Dr. R. W. Nurse (Building Research Station, Watford, Herts.). Secar 250, used in some experiments, is a high-alumina cement made from commercial calcined alumina. A typical composition is Al_2O_3, 71·7; CaO, 27·6; Fe_2O_3, 0·30; SiO_2, 0·25; ignition loss, 0·20; total, 100·05%; insoluble in HCl, 7·85; whence, CaO,Al_2O_3, 55·5; $CaO,2Al_2O_3$, 35·9; α-Al_2O_3 (corundum), 7·85%.

Phase-equilibrium Experiments.—Equilibrium was approached in different ways to obtain as much information as possible about both stable and unstable phases. Extreme care was always taken to avoid contamination by atmospheric carbon dioxide. Polythene bottles with screw caps and P.V.C. [poly(vinyl chloride)] gaskets were used, and were fitted with soda-lime guard tubes while the solid was being filtered off by suction through a covered Buchner funnel. With very few exceptions, this procedure was satisfactory. A room kept at 5° ± 0·5° was used for the work.

Supersaturated solutions were made by shaking Secar 250 (50 g.) with boiled distilled water (5 l.) for about 3 hr. and filtering. The clear filtrates generally had molar $CaO : Al_2O_3$ ratios slightly above 1, and contained about 1 g. of Al_2O_3 and 0·6 g. of CaO per l. Samples of the filtrate were analysed and weight aliquot parts of the rest taken in Polythene bottles, which were transferred to the 5° room and left for a day to cool. Precipitation did not usually occur during this time. Weighed amounts of solid calcium oxide were then added to the bottles, which were afterwards shaken continuously until the next batch was ready (never under a week), and then at least daily for the duration of the experiment. In a few experiments, lime solution was added to the supersaturated solutions, but this is inconvenient because the Al_2O_3 concentration is reduced. Addition of solid lime, although it does not reduce the Al_2O_3 concentration, also has disadvantages (see later). In some other experiments, no lime was added, the solutions being merely left to form precipitates. After suitable intervals the mixtures were filtered and the solutions analysed. $CaO : Al_2O_3$ ratios of solids were normally obtained by difference; a few solids were analysed directly, and the results agreed with those calculated.

Equilibrium was also approached by adding weighed amounts of $CaO,Al_2O_3,10H_2O$, $3CaO,Al_2O_3,6H_2O$, or hydrated alumina to water or lime solutions contained in Polythene bottles. Subsequent procedure was as with experiments starting from supersaturation. In all, 112 experiments were made, with times varying between 1 and 574 days.

Analytical Methods.—A few analyses were done by classical gravimetric procedures, but most were done by using edta (disodium salt of ethylenediaminetetra-acetic acid) to form complexes both with calcium and aluminium. Calcium was determined by back-titration at pH 10 with manganese(II), and aluminium by a slight modification of Haar and Bazen's method.[6] By these methods, it was possible to do duplicate CaO and Al_2O_3 analyses on a solution in about 30 min., with accuracies equal to those of the classical methods.

X-Ray Methods.—The solid products, and reference substances, were dried over saturated calcium chloride solution at room temperature, and *X*-ray powder photographs taken with 11·46 cm. diameter cameras with filtered copper radiation. Reference substances examined were $4CaO,Al_2O_3,13H_2O$, $2CaO,Al_2O_3,8H_2O$, $CaO,Al_2O_3,10H_2O$, $3CaO,Al_2O_3,6H_2O$,

[6] Haar and Bazen, *Analyt. Chim. Acta*, 1954, **10**, 23.

XUM

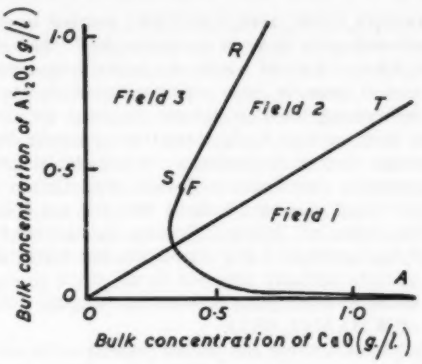
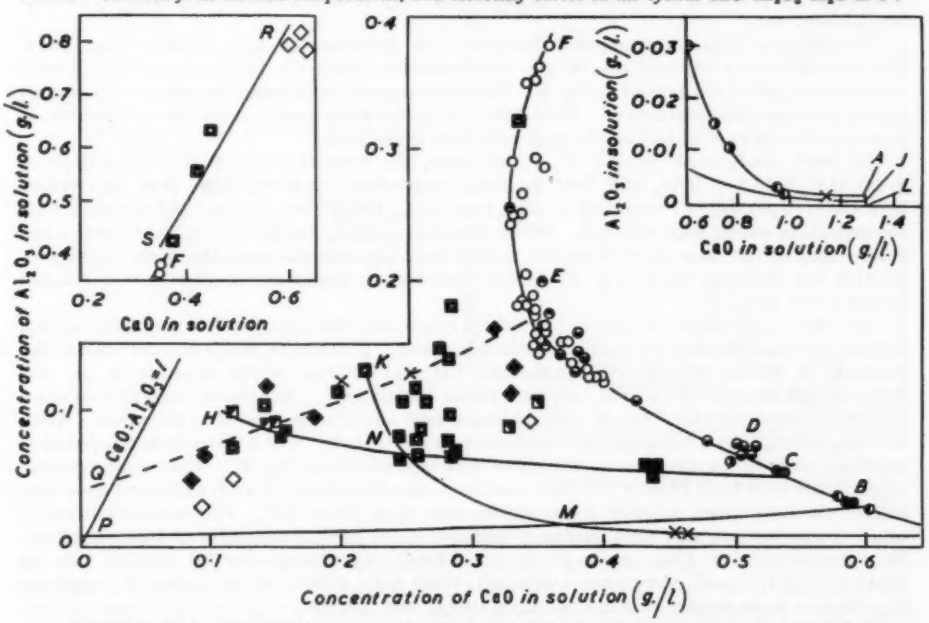


FIG. 1. *Definition of fields of bulk composition.*

AF is the metastable solubility curve of $4CaO,Al_2O_3,19H_2O$ and $2CaO,Al_2O_3,8H_2O$; *RS* is a line of slope $CaO : Al_2O_3$ (molar) = 1 passing close to *F*; *OT* is a line of slope $CaO : Al_2O_3$ (molar) = 3 passing through the origin.

FIG. 2. *Observed final solution compositions, and solubility curves in the system* $CaO–Al_2O_3–H_2O$ *at* 5°.*



Insets: continuations on different scales. For key to lettering see text. Key to experimental points:

	Solid phase(s) present	Starting material
●	$4CaO,Al_2O_3,19H_2O$	Supersaturated solution (field 1)
◐	"	$CaO,Al_2O_3,10H_2O$
◑	"	Alumina
◒	$4CaO,Al_2O_3,19H_2O$ + $2CaO,Al_2O_3,8H_2O$	Supersaturated solution (field 1)
○	$4CaO,Al_2O_3,19H_2O$ and/or $2CaO,Al_2O_3,8H_2O$ †	Supersaturated solution (field 2)
◓	" " " †	Supersaturated solution (field 3)
◥	$CaO,Al_2O_3,10H_2O$	Supersaturated solution (field 2)
■	"	$CaO,Al_2O_3,10H_2O$
□	$CaO,Al_2O_3,10H_2O$, usually + alumina	Supersaturated solution (field 3)
◩	$CaO,Al_2O_3,10H_2O$ + alumina	$CaO,Al_2O_3,10H_2O$
◊	Alumina	Supersaturated solution (field 3)
♦	Alumina	Alumina
×	$3CaO,Al_2O_3,6H_2O$	$3CaO,Al_2O_3,6H_2O$

* Trace constituents are sometimes ignored. † $CaO,Al_2O_3,10H_2O$ and/or alumina usually also present; $2CaO,Al_2O_3,8H_2O$ usually more abundant than $4CaO,Al_2O_3,19H_2O$.

$3CaO,Al_2O_3,CaCO_3,11H_2O$, $Ca(OH)_2$, calcite, bayerite, and gibbsite. In general, the patterns agreed well with those in the literature.[7] The alumina in the products was often very poorly crystallised. Except where the bayerite specimen had been used, and in certain other cases mentioned later, it gave a pattern most nearly resembling that of gibbsite. Occurrence of the two strong lines of gibbsite at about 4·8 and 4·4 Å, after allowance if necessary for the weak lines of $CaO,Al_2O_3,10H_2O$ in approximately the same positions, was regarded as the minimum test of its presence. It will be described simply as alumina. Powder patterns of preparations containing hydrated tetracalcium aluminate in contact with its mother-liquor showed basal spacings of about 10·6 and not 8 Å, confirming Roberts's view [8] that the shorter spacing arises on drying; Roberts showed that the compound in contact with solution was $4CaO,Al_2O_3,19H_2O$. For simplicity, the latter description will be used throughout, although the hydrate actually detected in the dried precipitates was $4CaO,Al_2O_3,13H_2O$. No attempt was made to distinguish between the slightly differing reported forms [1,8] of $4CaO,Al_2O_3,13H_2O$ and of $2CaO,Al_2O_3,8H_2O$.

In characterising the phases present in the solid products, account was taken of both *X*-ray and analytical evidence. With a few minor exceptions, the results of the two methods agreed satisfactorily, provided the difficulty of detecting very poorly crystallised phases by *X*-rays was allowed for.

Precipitation from Supersaturated Solutions.—(i) *Definition of fields of bulk composition.* For the description of these results it is convenient to divide the system into fields of bulk composition, which are defined in Fig. 1. The divisions are partly based on solubility and other curves subsequently established. The terms " bulk concentrations " imply the concentrations that would have existed had all the materials been in solution.

(ii) *Bulk compositions in field* 1. In all cases, the products were $4CaO,Al_2O_3,19H_2O$ or $2CaO,Al_2O_3,8H_2O$ or both, and final solution compositions were on *ADE* (Fig. 2). Where bulk $CaO : Al_2O_3$ (molar) exceeded 5, only $4CaO,Al_2O_3,19H_2O$ was formed, and the final CaO concentration was at least 0·53 g./l. Where bulk $CaO : Al_2O_3$ was 3—5, $2CaO,Al_2O_3,8H_2O$ and $4CaO,Al_2O_3,19H_2O$ were both formed. Comparison experiments with the same bulk composition but differing times (Fig. 3) showed that true or apparent equilibrium was reached within a few days.

(iii) *Bulk compositions in field* 2. In nearly every case, the solid product contained several phases, and equilibrium is evidently not easily reached. $2CaO,Al_2O_3,8H_2O$ was detected in the products of 32 out of the 35 experiments, $CaO,Al_2O_3,10H_2O$ in 25, alumina in 21, and $4CaO,Al_2O_3,19H_2O$ in 16 (usually only as a minor constituent). In several cases all four compounds occurred together, though with increased time one or more tended to disappear. With two exceptions, final solution compositions were on *DF* (Fig. 2). For a given bulk composition, solution compositions moved down this curve with increased time (Fig. 3). The two exceptional experiments were both of over 570 days' duration, and the results (Fig. 2) suggested that with sufficiently long times, solution compositions may drop below *DF*. The observed trend in solution composition with time implies a decrease in the $CaO : Al_2O_3$ ratio of the precipitate. In agreement with this, products of short-term experiments tended to be rich in $2CaO,Al_2O_3,8H_2O$ and sometimes contained $4CaO,Al_2O_3,19H_2O$ while those of long-term experiments were usually rich in $CaO,Al_2O_3,10H_2O$ and alumina.

(iv) *Bulk compositions in field* 3. The main product was usually $CaO,Al_2O_3,10H_2O$, often accompanied by alumina, and final solution compositions were mostly to the left of *CF* and on or above *HC* (Fig. 2). The alumina concentrations fell with time, and with many experiments of several months' duration the solution compositions were close to *HC*. The approach to equilibrium with a supersaturated solution to which no additional lime had been added is shown in Fig. 3. The points represent separate experiments with the same bulk composition but different times. Alumina was at first precipitated until the solution composition lay approximately on a line *RS*, which passes near *F* and has a slope corresponding to $CaO : Al_2O_3$ (molar) = 1. The composition of the precipitate was inferred from the change in solution composition, but it gave an anomalous and very weak *X*-ray pattern with the following spacings (Å) and relative intensities: 4·69 vw, 4·33 m, 3·88 s, 3·56 w, 3·30 m, 3·07 vw, 2·73 m, 2·07 w, 1·82 vw. It was not gibbsite or bayerite. $CaO,Al_2O_3,10H_2O$ was then precipitated, solution

[7] Lea, " The Chemistry of Cement and Concrete " (revised edition of Lea and Desch), Edward Arnold and Co. Ltd., London, 1956, Appendix III, p. 604.
[8] Roberts, *J. Appl. Chem.*, 1957, **7**, 543.

compositions moving down *RS* into the region to the left of *CF* and above *HC*. Beyond *S*, both $CaO,Al_2O_3,10H_2O$ and alumina were formed, with alumina tending to predominate. After 50—100 days, solution compositions approached a steady value a little above *HC*, and the precipitates were of $CaO,Al_2O_3,10H_2O$ mixed with badly crystallised gibbsite.

In a few experiments with bulk compositions near *RS*, traces of $2CaO,Al_2O_3,8H_2O$ or $4CaO,Al_2O_3,19H_2O$ were formed, together with alumina, and the solution compositions were on or near *DF* (Fig. 2). In others, where the bulk lime and alumina concentrations were both very low, alumina was formed with little or no $CaO,Al_2O_3,10H_2O$, and solution compositions were below point *H*; in one such case, the alumina was in the form of bayerite.

Treatment of $CaO,Al_2O_3,10H_2O$ *with Water or Lime Solutions.*—With water, $CaO,Al_2O_3,10H_2O$ dissolved incongruently, the solid products being unchanged $CaO,Al_2O_3,10H_2O$ and alumina.

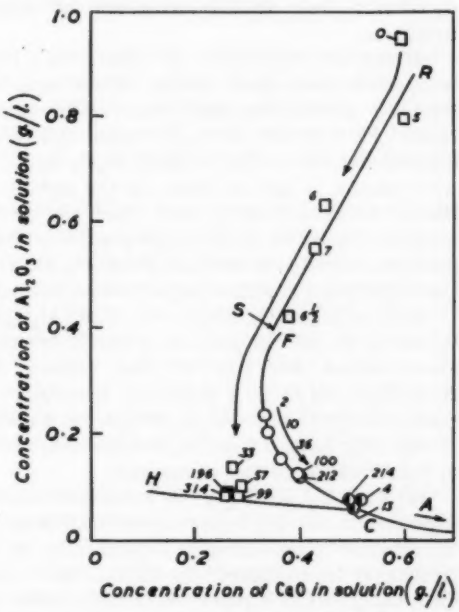


FIG. 3. *Course of precipitation from supersaturated solutions; three groups of experiments each with fixed bulk composition and varying times.*

Bulk compositions: ◐, CaO 2·053 g./l., Al_2O_3 0·768 g./l. (Field 1); ○, CaO 0·981 g./l., Al_2O_3 1·016 g./l. (Field 2); □, CaO 0·600 g./l., Al_2O_3 0·950 g./l. (Field 3). Time in days is shown against each point. Curves *HC*, *ACF*, and *RS* have the same significance as in Fig. 2.

Final solution compositions were near *H* (Fig. 2). With lime solutions containing initially 0·1—0·5 g. of CaO/l., it dissolved congruently or nearly so; final solution compositions were on *HC*, and the solids were unchanged $CaO,Al_2O_3,10H_2O$. With lime solutions containing initially more than 0·8 g. of CaO/l., the solids consisted chiefly of $4CaO,Al_2O_3,19H_2O$, and solution compositions were on *AC*; small proportions of alumina and $3CaO,Al_2O_3,6H_2O$ were sometimes also formed. Comparison of experiments with similar bulk compositions and different times suggested that apparent equilibrium was probably always reached within about 30 days.

Treatment of Alumina with Lime Solutions.—Where hydrated alumina was treated with lime solutions containing 0·1—0·5 g. of CaO/l., it persisted largely unaltered in the products, and final solution compositions were near an ill-defined curve *QE* (Fig. 2). With lime solutions containing more than 0·8 g. of CaO/l., the products contained unchanged alumina and $4CaO,Al_2O_3,19H_2O$, and final solution compositions were on *AD* (Fig. 2).

Treatment of $3CaO,Al_2O_3,6H_2O$ *with Water or Lime Solutions.*—This compound dissolved congruently in water or in lime solutions. Final solution compositions (Fig. 2) lay approximately on the solubility curve *JK* obtained at 21° by Wells, Clarke, and McMurdie.[9] From one pair of experiments, equilibrium seemed to be established within about 30 days.

[9] Wells, Clarke, and McMurdie, *J. Res. Nat. Bur. Stand.*, 1943, **30**, 367.

Discussion

Stable Equilibria.—Because of the persistence of metastable phases, very few of the present results relate to thermodynamically stable equilibria. It nevertheless seems fairly safe to infer from results obtained at higher temperatures [3, 9] that the stable compounds in the system at 5° are gibbsite, $3CaO,Al_2O_3,6H_2O$, and calcium hydroxide, and also that the solubility curves of the first two of these do not differ much from those obtained at 21°. In the case of $3CaO,Al_2O_3,6H_2O$ this view is supported by the present results. On this basis curves are included in Fig. 2 for gibbsite (*PMB*) and for $3CaO,Al_2O_3,6H_2O$ (*KMJ*). The short solubility curve *AJL* for calcium hydroxide is inferred from the known solubility at 5°.[10] Curves *PM*, *MJ*, and *JL* thus relate to stable equilibria; their prolongations, and all other curves in Fig. 2, relate to metastable equilibria.

Metastable Equilibria.—(i) $4CaO,Al_2O_3,19H_2O$ *and* $2CaO,Al_2O_3,8H_2O$. These two compounds have closely similar crystal structures, and it is not easy to distinguish their solubility curves from each other. The curve *ADF* (Fig. 2) is associated with both of them. Its lime-rich end is the metastable solubility curve of $4CaO,Al_2O_3,19H_2O$, and its alumina-rich end is that of $2CaO,Al_2O_3,8H_2O$. The triple point for these two compounds with solution is hard to locate, as the curve seems continuous and there is a considerable portion between *D* and *E* over which the three phases can co-exist for a long time. The most likely position for the triple point is perhaps near *D*, which corresponds to the highest lime concentration at which $2CaO,Al_2O_3,8H_2O$ was found. The same difficulty in locating this triple point occurs at higher temperatures.[1, 2, 9]

Both $4CaO,Al_2O_3,19H_2O$ and $2CaO,Al_2O_3,8H_2O$ are purely metastable phases in this system at 5°, but the first has a relatively stable field of existence at CaO concentrations above about 0·5 g./l. It was formed from both under- and over-saturation. $2CaO,Al_2O_3,8H_2O$ is a relatively transitory product; at certain concentrations it is stable relative to $4CaO,Al_2O_3,19H_2O$, but it is always unstable relative to $CaO,Al_2O_3,10H_2O$. It was only formed from supersaturation, and usually occurred as an intermediate stage in the formation of that compound.

(ii) $CaO,Al_2O_3,10H_2O$. A metastable solubility curve *HC* (Fig. 2) is established from experiments starting from undersaturation and from supersaturation. In the former case the solution compositions lie substantially on the curve, while in the latter the curve can reasonably be considered to be the limit which they approach if given enough time. $CaO,Al_2O_3,10H_2O$ is purely metastable in the system at 5°, but it is persistent and stable relative to $2CaO,Al_2O_3,8H_2O$ and $4CaO,Al_2O_3,19H_2O$ at CaO concentrations below about 0·5 g./l. At higher lime concentrations, it reacts with the solution, giving mainly $4CaO,Al_2O_3,19H_2O$. There is a slight tendency to form the stable phases, $3CaO,Al_2O_3,6H_2O$ and alumina.

(iii) *Alumina.* The alumina formed or used was always imperfectly crystallised, and as improvement in crystallinity was slow, no definite solubility curve could be obtained. An infinite family of unstable curves lying above that of fully crystalline gibbsite (Fig. 2, *PB*) can be envisaged. The ill-defined curve *QE* obtained in the present work is a typical one for moderately well-crystallised hydrated alumina. It applies approximately both to the bayerite specimen and to the alumina formed by using $CaO,Al_2O_3,10H_2O$ as starting material. With alumina formed in long-term experiments starting from supersaturation the Al_2O_3 concentrations in solution were lower.

Triple Points.—These are listed in the Table. All but the first two relate to metastable equilibria. Gibbsite implies well-crystallised natural material, and alumina implies the typical synthetic material (bayerite or gibbsite) mentioned above.

Variable Solubilities.—The effect of varying crystallinity on the apparent solubility of alumina has already been discussed; alumina concentrations were high relative to the assumed position of the stable gibbsite curve whether equilibrium was approached from

List of triple points.

Phases (in addition to solution)	Ref. letter on Fig. 2	Solution composition (g./l.) CaO	Al_2O_3
$Ca(OH)_2$–$3CaO,Al_2O_3,6H_2O$	*J*	1·28	<0·002
$3CaO,Al_2O_3,6H_2O$–gibbsite	*M*	0·4 app.	0·02 app.
$Ca(OH)_2$–$4CaO,Al_2O_3,19H_2O$	*A*	1·28	<0·002
$4CaO,Al_2O_3,19H_2O$–gibbsite	*B*	0·59 app.	0·04 app.
$4CaO,Al_2O_3,19H_2O$–$CaO,Al_2O_3,10H_2O$	*C*	0·53	0·06
$4CaO,Al_2O_3,19H_2O$–$2CaO,Al_2O_3,8H_2O$	*D*	0·51	0·07
$2CaO,Al_2O_3,8H_2O$–alumina *	*E*	0·35	0·17
$CaO,Al_2O_3,10H_2O$–alumina *	*H*	0·14	0·09
$3CaO,Al_2O_3,6H_2O$–alumina *	*K*	0·22	0·12
$3CaO,Al_2O_3,6H_2O$–$CaO,Al_2O_3,10H_2O$	*N*	0·25	0·07

* Position variable depending on crystallinity of alumina.

under- or over-saturation. With calcium hydroxide, also, the apparent solubility depends on particle size, though to a smaller extent.[10] With $2CaO,Al_2O_3,8H_2O$ and $4CaO,Al_2O_3,19H_2O$ there was no evidence of variable solubility. In nearly every case where either compound was formed, whether or not other solid phases were there as well, the solution compositions lay on *ADF*. This is readily explained by the fact that both compounds crystallise relatively well.

With $CaO,Al_2O_3,10H_2O$, high apparent solubilities were generally obtained when equilibrium was approached from supersaturation. This could be described either as slowness in reaching equilibrium, or in terms of a series of unstable solubility curves lying above the metastable one *HC*. The second description appears reasonable, as $CaO,Al_2O_3,10H_2O$ crystallises very poorly. From this viewpoint, the metastable solubility curve *DF* of $2CaO,Al_2O_3,8H_2O$ is also the locus of the unstable triple point for this compound with solution and poorly crystallised forms of $CaO,Al_2O_3,10H_2O$. The line *RS* (Figs. 2 and 3) similarly represents a band of unstable triple points for solution with poorly crystallised forms of $CaO,Al_2O_3,10H_2O$ and alumina. The alumina in this case is not gibbsite or bayerite, but the unstable form giving the abnormal *X*-ray pattern described previously.

The Approach to Equilibrium from Supersaturation.—For bulk compositions in field 2, the $CaO : Al_2O_3$ ratio of the precipitate decreases markedly with time (Fig. 3). This can be attributed to the conditions under which precipitation occurs. Addition of calcium hydroxide solution, or especially of solid calcium oxide, to a supersaturated solution necessarily produces regions of high lime concentration, and it is in these regions that precipitation begins. The initial precipitates are therefore of higher $CaO : Al_2O_3$ ratio than those eventually formed, and the dissolution of the high-lime compounds and formation of those of lower $CaO : Al_2O_3$ ratio are slow processes. The same effect probably explains the formation and persistence of $4CaO,Al_2O_3,19H_2O$ in cases where the bulk composition is in field 1 and the final solution composition above point *D* on curve *ADF* (Fig. 2). Dissolution of $4CaO,Al_2O_3,19H_2O$ and formation of $2CaO,Al_2O_3,8H_2O$ seem to be very slow in the range *DE* just above the triple point.

Comparison of Results with Those obtained at Higher Temperatures.—In Fig. 4, the solubility curves for $4CaO,Al_2O_3,19H_2O$–$2CaO,Al_2O_3,8H_2O$, $3CaO,Al_2O_3,6H_2O$, and $Ca(OH)_2$ at 5° are compared with ones obtained at higher temperatures.[3, 9, 11] The solubility curve for $4CaO,Al_2O_3,19H_2O$ and $2CaO,Al_2O_3,8H_2O$ rises sharply with temperature; at 90°, these compounds change so rapidly into $3CaO,Al_2O_3,6H_2O$ that true metastable solubility curves are unobtainable. The solubility curve of $3CaO,Al_2O_3,6H_2O$ also rises with temperature, though less markedly; the results for 5°, 21°, 25°, and even 50° are almost identical. The solubility of calcium hydroxide falls steadily with rising temperature.[10]

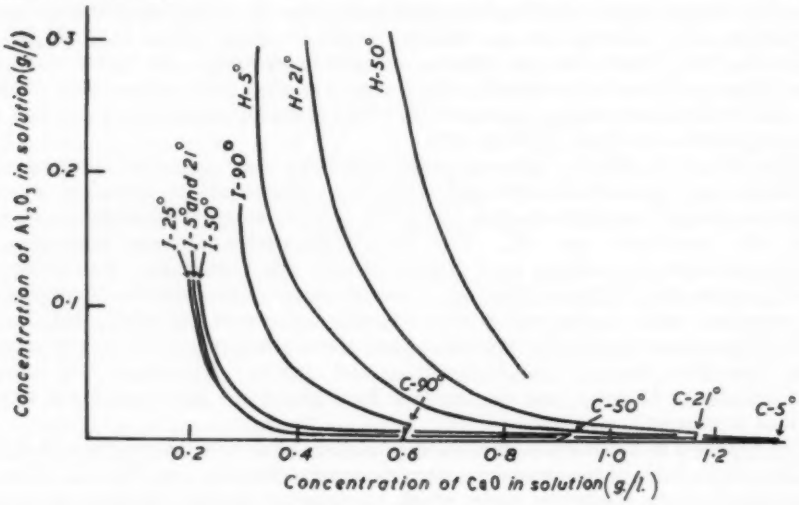
At 21° $4CaO,Al_2O_3,19H_2O$ and $2CaO,Al_2O_3,8H_2O$ change fairly quickly into

[10] Bassett, *J.*, 1934, 1270.

$3CaO,Al_2O_3,6H_2O$ when suspended in aqueous solutions; Wells, Clarke, and McMurdie [9] found that out of 48 experiments starting from supersaturation, 21 gave amounts of $3CaO,Al_2O_3,6H_2O$ detectable by microscope within 10 days. In the present work at 5°, no experiments of this type gave $3CaO,Al_2O_3,6H_2O$, even in more than 570 days. This compound was indeed formed in only three experiments of any kind, all starting from $CaO,Al_2O_3,10H_2O$. In these it was only a minor product.

$CaO,Al_2O_3,10H_2O$ was apparently not formed in any of Wells, Clarke, and McMurdie's experiments in the course of their extensive investigation at 21°, and no metastable

FIG. 4. *Influence of temperature on the stable or metastable solubility curves of* $4CaO,Al_2O_3,19H_2O$–$2CaO,Al_2O_3,8H_2O$ (marked *H*), $3CaO,Al_2O_3,6H_2O$ (marked *I*), and $Ca(OH)_2$ (marked *C*). Sources of data: 5°, this investigation; 21° and 90°, Wells, Clarke, and McMurdie; [9] 50°, Peppler and Wells; [3] 25°, Bessey.[11]



solubility curve for it at this or any other temperature has previously been reported. At 5°, however, a curve can be obtained, and in the absence of well-crystallised alumina, part of this curve (*HN*, Fig. 2) is stable, not only relative to that of $2CaO,Al_2O_3,8H_2O$ but also relative to that of $3CaO,Al_2O_3,6H_2O$. A line through the origin with slope $CaO : Al_2O_3$ (molar) = 1 passes to the left of *H*; treatment of anhydrous or hydrated monocalcium aluminate with excess of water at 5° therefore gives a virtually stable mixture of $CaO,Al_2O_3,10H_2O$ and alumina, as long as the alumina and $CaO,Al_2O_3,10H_2O$ curves intersect to the left of *N*. If the crystallinity of the alumina approaches that of stable gibbsite, dissolution of $CaO,Al_2O_3,10H_2O$ and formation of $3CaO,Al_2O_3,6H_2O$ are liable to occur.

Detailed Analytical and X-Ray Results.—Detailed analytical and *X*-ray data can be obtained from the authors.

We thank the Lafarge Aluminous Cement Company for financial support; also Dr. T. D. Robson of that Company, and Dr. R. W. Nurse, Dr. F. E. Jones, and their colleagues (Building Research Station, Watford, Herts.), for helpful discussions and for material.

UNIVERSITY OF ABERDEEN. [*Received, October 18th,* 1957.]

[11] Bessey, *Proc. Symp. Chem. Cements, Stockholm,* 1938, 178.

434. *Alicyclic Glycols. Part XVI.* Decalin 2 : 3-Ketols.*

By Md. Erfan Ali and L. N. Owen.

A new route to each stereoisomer of *cyclo*hexane-1 : 2-diacetic acid is described. Acyloin cyclisation of the *cis*- and the *trans*-dimethyl ester leads to 2 : 3-ketols in the *cis*- and the *trans*-decalin series. Elimination of the keto-group furnishes the corresponding decalol and enables an assignment of configuration to be made to the hydroxyl group in each ketol; the results are in accordance with conformational requirements.

In connection with studies on the decalin-2 : 3-diols, reported in the following paper, convenient sources of the 3-oxodecalin-2-ols were required. By hydrolysis of 2-chloro-3-oxo-*trans*-decalin Lehmann and Krätschell [1] obtained two ketols, m. p.s 84° and 134°, and by a similar method in the *cis*-series Cook and Lawrence [2] prepared one, m. p. 88—90°, of the two possible *cis*-fused isomers; the higher-melting ketol in the *trans*-series was also obtained [3] by reduction of *trans*-decalin-2 : 3-dione, but no configuration was allocated to the hydroxyl group in any of these compounds. In our hands, Lehmann and Krätschell's procedure gave only one product, m. p. 82°. The overall yields from the decalones are very poor, and an alternative approach was therefore desirable.

An obvious synthetical route is the acyloin cyclisation of an ester of *cyclo*hexane-1 : 2-diacetic acid, but when the present investigation was begun neither the *cis*- nor the *trans*-acid was readily obtainable in quantity, both having been prepared hitherto by oxidation of Δ^2-octalin or of suitable oxygenated decalin derivatives; very recently Stork and Hill [4] have reported an improved method for the *cis*-acid which involves the ozonolysis of an oxalyl derivative of *cis*-decalin-2-one. Attempts to apply the Arndt–Eistert method to *cyclo*hexane-*cis*-1 : 2-dicarboxyl chloride were unpromising, but the availability of the two stereoisomers of 1 : 2-bishydroxymethyl*cyclo*hexane [5] opened a new and convenient route. By reaction of the *trans*-ditoluene-*p*-sulphonate (I) with potassium cyanide in ethanol the dinitrile (II) and a small amount of the ethoxy-nitrile (III) were obtained; hydrolysis of the former gave *cyclo*hexane-*trans*-1 : 2-diacetic acid in good yield. The *cis*-ditoluene-*p*-sulphonate was similarly converted into the *cis*-acid, the *cis*-ethoxy-nitrile (V) being obtained as a by-product at the intermediate stage. Hydrolysis of each ethoxy-nitrile (III) and (V) with boiling 50% sulphuric acid gave the same lactonic product, as shown by the formation of identical *S*-benzyl*iso*thiuronium salts of the corresponding hydroxy-acid. The most likely explanation of the change in configuration which must have occurred with one isomer is that under the vigorous conditions elimination occurs to give the unsaturated acid (IV), which could then give either a γ- or a δ-lactone. The infrared spectrum showed a peak at 1735 cm.$^{-1}$ characteristic of a δ-lactone, and the product is therefore formulated as the lactone (VI) of (*cis* or *trans*)-2-hydroxymethyl*cyclo*hexylacetic acid. In acyclic γ-unsaturated acids with a terminal double bond lactonisation occurs preferentially at the γ- rather than the δ-position,[6] but in the present instance the production of a bicyclic system evidently favours the formation of a second six-membered ring.

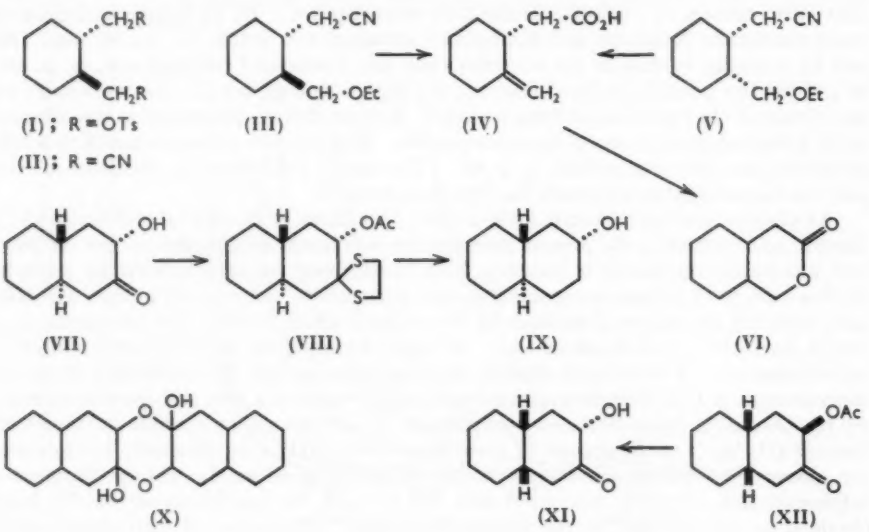
By the use of Sheehan's [7] convenient modification of the acyloin cyclisation, dimethyl *cyclo*hexane-*trans*-1 : 2-diacetate was converted in 70% yield into a ketol, m. p. 82—83°, identical with that obtained from 3-chloro-*trans*-decalin-2-one. The presence of a

* Part XV, Ali and Owen, *J.*, 1958, 1074.

[1] Lehmann and Krätschell, *Ber.*, 1934, **67**, 1857.
[2] Cook and Lawrence, *J.*, 1937, 817.
[3] Ganapathi, *J. Indian Chem. Soc.*, 1938, **15**, 407.
[4] Stork and Hill, *J. Amer. Chem. Soc.*, 1957, **79**, 495.
[5] Haggis and Owen, *J.*, 1953, 389.
[6] Linstead and Rydon, *J.*, 1933, 580.
[7] Sheehan and Coderre, *J. Amer. Chem. Soc.*, 1953, **75**, 3997.

XUM

carbonyl and a hydroxyl group was shown by the infrared spectrum and confirmed by the preparation of a semicarbazone, a 2 : 4-dinitrophenylosazone, a toluene-*p*-sulphonate, a 3 : 5-dinitrobenzoate, an acetate (from which the same ketol was regenerated on deacetylation), and an acetate 2 : 4-dinitrophenylhydrazone; oxidation with bismuth trioxide [8] gave *trans*-decalin-2 : 3-dione. Lehmann and Krätschell [1] reported failure to acetylate their ketols, and claimed to have obtained the lower-melting ketol from the isomer by treatment with toluene-*p*-sulphonyl chloride in pyridine; it is difficult to understand why they did not obtain the toluene-*p*-sulphonate under these conditions. The ketol showed no tendency to enolise, since it gave no colour with ferric chloride, and its infrared spectrum was devoid of absorption attributable to an ethylenic linkage.



In the double-chair form of the *trans*-decalin system each hydrogen atom or substituent has one definite conformation, axial or equatorial, which is determined by its configuration, and the isolation of only one of the two possible ketols suggested that this was the 2α-compound (VII),* in which the hydroxyl group is in the more stable equatorial position; † the configurational stability of the ketol was confirmed by its resistance towards epimerisation by sodium ethoxide. The position of the C–O stretching band in the infrared spectrum of sterols has been shown to depend upon the conformation of the hydroxyl group, an equatorial and an axial disposition giving rise to absorption at *ca.* 1040 and *ca.* 1000 cm.$^{-1}$, respectively.[9,10] The absorption of the acetates is also characteristic, those with an equatorial group giving a single band in the 1200—1250 cm.$^{-1}$ region,

* In this and the following paper the designations α and β are used to indicate configurations in the same sense as in the steroid field, the decalin skeleton being always represented with a β-orientated hydrogen atom at $C_{(9)}$.

† It seems unlikely that dipole interaction between the equatorial hydroxyl and the carbonyl group, which it almost eclipses, would be sufficiently strong to favour the axial conformation, as occurs with certain bromo-ketones (cf. ref. 15); the equatorial conformation would also permit stabilisation by hydrogen bonding.

[8] Rigby, *J.*, 1951, 793.

[9] Cole, Jones, and Dobriner, *J. Amer. Chem. Soc.*, 1952, **74**, 5571; Rosenkrantz, Milhorat, and Farber, *J. Biol. Chem.*, 1952, **195**, 509.

[10] Fürst, Kuhn, Scotoni, and Gunthard, *Helv. Chim. Acta*, 1952, **35**, 951; Braude and Waight in "Progress in Stereochemistry", ed. Klyne, Butterworths, 1954, Vol. I, p. 126.

whilst for an axial conformation the band is complex.[10,11] For the decalols the distinction is not so clearly defined, though their acetates conform to the above generalisation.[12] The infrared spectrum of the ketol (VII) showed no band near 1000 cm.$^{-1}$, but several between 1025 and 1087 cm.$^{-1}$; the acetate showed a strong single maximum at 1233 cm.$^{-1}$. These results therefore supported the α-configuration, and confirmatory chemical evidence was provided by reaction of the ketol acetate with ethane-1 : 2-dithiol, and desulphurisation of the product (VIII) to give, after deacetylation, *trans*-decalin-2α-ol (IX), the configuration of which rests on a sound basis.[12]

When the product from the acyloin reaction was worked up under acidic conditions a very sparingly soluble compound was obtained instead of the ketol; it was also slowly formed when the pure ketol was stored, and more rapidly from the crude ketol. It showed no carbonyl band in the infrared spectrum and gave no immediate reaction with 2 : 4-dinitrophenylhydrazine, but when heated with this reagent it gave the 2 : 4-dinitrophenylosazone of *trans*-decalin-2 : 3-dione and was readily converted into the dione by oxidation with bismuth trioxide. With pyridine–acetic anhydride at 100° it gave the monomeric ketol acetate identical with that described above. Although the apparent molecular weight (Rast method) was approximately that of the monomeric ketol this is no doubt due to dissociation by heat, and the compound is evidently the dimer (X) analogous to that formed [13] from 2-hydroxy*cyclo*hexanone.

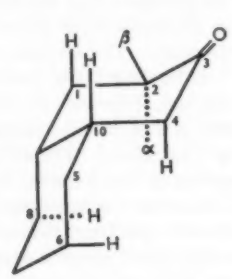
Unlike the reaction in the *trans*-series, the acyloin cyclisation of dimethyl *cyclo*hexane-*cis*-1 : 2-diacetate gave a mixture. One product, m. p. 89—90°, isolated in 27% yield, was a monomeric ketol which gave derivatives of the keto- and the hydroxy-function, but the infrared spectrum, which included a group of bands with frequencies ranging from 1010 to 1087 cm.$^{-1}$, was not configurationally decisive. The acetate, m. p. 74—75°, however, showed a strong *single* peak at 1227 cm.$^{-1}$, indicating [12] the α-configuration, and this was confirmed by reaction with ethane-1 : 2-dithiol, followed by desulphurisation and deacetylation to give *cis*-decalin-2α-ol. The ketol is therefore 3-oxo-*cis*-decalin-2α-ol (XI), and is probably identical with that described by Cook *et al.*[2] The second product isolated was a dimer, which showed no carbonyl absorption in the infrared region, but this compound was not derived from the ketol (XI) since on vigorous acetylation it gave an isomeric ketol acetate, m. p. 98—99°, whose infrared spectrum differed significantly from that of the lower-melting isomer in that the acetate band showed *twin* peaks at 1231 and 1223 cm.$^{-1}$, consistent [12] with a β-configuration (XII). Each acetate gave an individual 2 : 4-dinitrophenylhydrazone, and, with an excess of the reagent, the same 2 : 4-dinitrophenylosazone of *cis*-decalin-2 : 3-dione. An interesting observation was that the 2α- and the 2β-acetate by solvolysis in the presence of sodium ethoxide gave the same 3-oxo-*cis*-decalin-2α-ol (XI). In the flexible *cis*-decalin system there are two interconvertible double-chair forms, and in passing from one to the other an axially disposed group becomes equatorial and *vice versa*. Consequently a hydroxyl group in either the 2α- or the 2β-configuration can take up the stable equatorial position, and at first sight the exclusive formation of the one isomer (XI) from both acetates under epimerisation conditions seems unexpected. It is necessary, however, to take account of the important non-bonded interactions which occur between certain axially disposed groups attached to different rings.[14] In conformation (XIII) of the 2α-ketol (α = OH; β = H) there are three such interactions, *viz.*, $O_{(2)}$–$H_{(8)}$, $H_{(8)}$–$H_{(4)}$, and $H_{(4)}$–$H_{(6)}$, and in the first of these the oxygen–hydrogen distance (centre to centre) is only 1·7 Å, a situation which must result in

[11] Jones, Humphries, Herling, and Dobriner, *J. Amer. Chem. Soc.*, 1951, **73**, 3215; Jones and Herling, *ibid.*, 1956, **78**, 1152.
[12] Dauben, Hoerger, and Freeman, *J. Amer. Chem. Soc.*, 1952, **74**, 5206.
[13] Sheehan, O'Neill, and White, *ibid.*, 1950, **70**, 3376.
[14] Mills, *J.*, 1953, 260; Dauben, Tweit, and Mannerskantz, *J. Amer. Chem. Soc.*, 1954, **76**, 4420; Dauben and Pitzer, Ch. 1 of "Steric Effects in Organic Chemistry," ed M. S. Newman, Chapman and Hall Ltd., 1956.

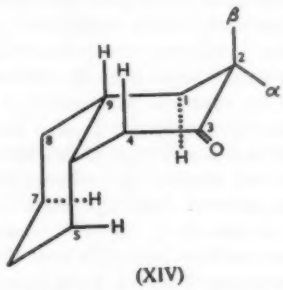
XUM

considerable steric repulsion; the distance between the hydrogen atoms involved in the other two is 1·85 Å, which would result in smaller but still significant repulsions each equivalent to a skew-butane interaction. The alternative conformation (XIV) exhibits only the two interactions $H_{(5)}$–$H_{(1)}$ and $H_{(1)}$–$H_{(7)}$ (there being no inter-ring effect involving the carbonyl group [15]), and furthermore lacks the ordinary 1 : 3-diaxial repulsion $O_{(2)}$–$H_{(4)}$ present in (XIII). With the 2β-ketol (α = H; β = OH), conformation (XIII) has three inter-ring repulsions, $H_{(2)}$–$H_{(8)}$, $H_{(8)}$–$H_{(4)}$, and $H_{(4)}$–$H_{(6)}$, whilst (XIV) has $H_{(5)}$–$H_{(1)}$ and $H_{(1)}$–$H_{(7)}$ plus the two ordinary diaxial interactions $O_{(2)}$–$H_{(4)}$ and $O_{(2)}$–$H_{(9)}$. Although some interaction may occur between the carbonyl group and an equatorial hydroxyl at $C_{(2)}$ (as mentioned above in connection with the *trans*-decalin isomer), this would be the same for both the 2α-ketol in conformation (XIV) and the 2β-ketol in conformation (XIII). Thus, of the four possibilities, the 2α-ketol in conformation (XIV) would be expected to be the most stable, having one fewer skew-butane interaction than the 2β-ketol in conformation (XIII).

Some further points arising from the spectroscopic results are of interest. In agreement with the conclusions, by Dickson and Page,[16] that a vicinal acetoxy-group, whether axial or equatorial, raises the C=O stretching frequency, the three ketol acetates all showed a carbonyl absorption maximum at 1733 cm.$^{-1}$, compared with *ca.* 1720 cm.$^{-1}$ for *cis*- and *trans*-decalin-2-one.[17] The C=O and C–O stretching frequencies in the acetate group, which in the three compounds were at *ca.* 1750 and 1230 cm.$^{-1}$ respectively, also showed the expected [16] displacement from the normal values (*ca.* 1730 and 1240 cm.$^{-1}$).



(XIII)



(XIV)

In the ultraviolet region, the weak carbonyl band in a simple steroid ketone at *ca.* 280 mμ is displaced to a lower wavelength by a vicinal equatorial hydroxyl or acetoxy-group, to the extent of *ca.* 12 mμ and 5 mμ respectively.[18] Both *cis*- and *trans*-decalin-2-one show this band at 283 mμ; [19,20] the maxima for the *cis*- and the *trans*-decalin ketol were at 273 and 275 mμ, respectively, in good agreement with prediction, but the two stereoisomeric *cis*-decalin ketol acetates both showed a maximum at 282 mμ and the *trans*-decalin ketol acetate one at 287 mμ. Since, from the arguments advanced above, the vicinal group in all these compounds is in the equatorial position, the generalisation evidently cannot be safely applied to acetates, though it is still true that acetylation of the equatorial hydroxyl group in the ketols results in a marked shift of the carbonyl band to a longer wavelength.

Experimental

Microanalyses in this and the following paper were by Miss J. Cuckney and staff, and absorption spectra by Mr. R. L. Erskine, B.Sc., A.R.C.S., and Mrs. A. I. Boston.

[15] Klyne, *Experientia*, 1956, **12**, 119.
[16] Dickson and Page, *J.*, 1955, 447.
[17] Lecomte, *J. Phys. Radium*, 1945, **6**, 257.
[18] Cookson and Dandegaonker, *J.*, 1955, 352; Baumgartner and Tamm, *Helv. Chim. Acta*, 1955, **38**, 441.
[19] Biquard, *Bull. Soc. chim. France*, 1941, **8**, 725.
[20] Tsatsas, *Ann. Chim.*, 1944, **19**, 247.

trans-*Decalin*-2 : 3-*dione* 2 : 4-*Dinitrophenylosazone*.—The diketone, prepared by Ganapathi's [3] method, had m. p. 99—100° (lit.,[3] m. p. 99—100°); $\lambda_{max.}$ in ethanol 269 mμ (ε 7500); disemicarbazone, m. p. 264° (lit.,[3] m. p. 264—265°). Reaction with 2 : 4-dinitrophenylhydrazine (2 mol.) in methanolic sulphuric acid for a few minutes under reflux gave red needles (from chloroform–methanol) of the 2 : 4-*dinitrophenylosazone*, m. p. 218—219° (decomp.) (Found: C, 50·4; H, 4·45; N, 21·5. $C_{22}H_{22}O_8N_8$ requires C, 50·2; H, 4·2; N, 21·3%); $\lambda_{max.}$ in chloroform 243, 260, 353, 400 mμ (ε 21,000, 21,500, 34,000, 24,000, respectively).

Reaction of 2-*Chloro*-3-*oxo*-trans-*decalin with Aqueous Sodium Hydroxide*.—The chloroketone [20] (3·4 g.) was boiled under reflux for 1 hr. with a deficiency (70 c.c.) of 1% aqueous sodium hydroxide, according to the conditions described by Lehmann and Krätschell.[1] The mixture, which had become neutral, was cooled, and the solid (2·6 g.), m. p. 63—69°, was collected; it contained halogen. Fractional crystallisation from methanol and from aqueous methanol gave only 3-oxo-*trans*-decalin-2α-ol (1·2 g.), m. p. and mixed m. p. 82°, and a trace of the dimer, m. p. 122° (see below). Evaporation of the mother liquors, and recrystallisation of the residue from light petroleum (b. p. 60—80°), gave more ketol (0·2 g.), m. p. 82°. The halogen-containing residue obtained by evaporation of the petroleum mother liquors was re-treated with boiling alkali as before, and gave a further quantity (0·3 g.) of ketol, m. p. 80—82°. No higher-melting epimer was encountered.

Ditoluene-p-*sulphonates of* 1 : 2-*Bishydroxymethyl*cyclo*hexane*.—Improved yields were obtained by a modification of the original [5] method. The *trans*-diol (71·5 g.) in dry pyridine (260 c.c.) was added drop by drop to a vigorously stirred solution of toluene-*p*-sulphonyl chloride (215 g.) in dry pyridine (450 c.c.) at 0° during 4 hr. The stirring was continued for 2 hr. at room temperature, and the mixture was then poured into ice-water. The precipitate was washed with water and recrystallised from methanol to give the *trans*-ditoluene-*p*-sulphonate (200 g., 89%), m. p. 108° (lit.,[5] m. p. 108°).

The *cis*-ditoluene-*p*-sulphonate, m. p. 83—84° (lit.,[5] m. p. 84—85°), was similarly prepared (yield, 68%) from *cis*-1 : 2-bishydroxymethyl*cyclo*hexane.

trans-1 : 2-*Biscyanomethyl*cyclo*hexane*.—The *trans*-ditoluene-*p*-sulphonate (200 g.), potassium cyanide (83·5 g.), ethanol (1200 c.c.), and water (120 c.c.) were boiled under reflux for 60 hr. The alcohol was then removed under reduced pressure and the residue was diluted with water and extracted with ether. Removal of solvent from the dried (Na_2SO_4) extract, followed by careful distillation of the residue through a short Vigreux column, gave (i) 3·7 g., b. p. 90—108°/0·4 mm., and (ii) trans-1 : 2-*biscyanomethyl*cyclo*hexane* (49·5 g., 69%), b. p. 143—144°/0·4 mm., n_D^{19} 1·4829 (Found: C, 73·6; H, 8·8; N, 17·1. $C_{10}H_{14}N_2$ requires C, 74·0; H, 8·7; N, 17·3%). Redistillation of (i) gave trans-2-*ethoxymethyl*cyclo*hexylmethyl cyanide*, b. p. 76°/0·2 mm., n_D^{20} 1·4600 (Found: C, 72·8; H, 10·4; N, 7·85. $C_{11}H_{19}ON$ requires C, 72·9; H, 10·6; N, 7·7%).

cyclo*Hexane*-trans-1 : 2-*diacetic Acid*.—A mixture of *trans*-1 : 2-biscyanomethyl*cyclo*hexane (49·5 g.) and 50% sulphuric acid (1200 c.c.) was boiled under reflux for 8 hr. The mixture was cooled and the solid, m. p. 166—167°, was collected and recrystallised from aqueous methanol to give *cyclo*hexane-*trans*-1 : 2-diacetic acid (50 g., 82%), m. p. 167° (lit.,[21] m. p. 167°).

Dimethyl cyclo*Hexane*-trans-1 : 2-*diacetate*.—The acid (30 g.), dry methanol (19 g.), dry benzene (56 c.c.), and concentrated sulphuric acid (9 g.) were boiled under reflux overnight. Water was then added and the benzene layer was washed with aqueous sodium hydrogen carbonate, and water, and dried (Na_2SO_4). Removal of the solvent and distillation of the residue gave the trans-*dimethyl ester* (30·8 g., 90%), b. p. 115°/0·7 mm., n_D^{19} 1·4625 (Found: C, 62·95; H, 8·9. $C_{12}H_{20}O_4$ requires C, 63·1; H, 8·8%).

cis-1 : 2-*Biscyanomethyl*cyclo*hexane*.—A mixture of *cis*-1 : 2-bishydroxymethyl*cyclo*hexane ditoluene-*p*-sulphonate (163·5 g.), potassium cyanide (70 g.), ethanol (900 c.c.), and water (90 c.c.) was boiled under reflux for 24 hr. The product was isolated as described for the corresponding *trans*-compound, and was distilled through a short Vigreux column to give (i) 7·5 g., b. p. 50—130°/0·2 mm., and (ii) the cis-*dinitrile* (23·1 g., 39·4%), b. p. 130°/0·2 mm., n_D^{20} 1·4865 (Found: C, 74·1; H, 8·9; N, 17·6. $C_{10}H_{14}N_2$ requires C, 74·0; H, 8·7; N, 17·3%). The lower-boiling fraction on redistillation gave cis-2-*ethoxymethyl*cyclo*hexylmethyl cyanide* (2 g.), b. p. 70°/0·2 mm., n_D^{21} 1·4624 (Found: C, 72·6; H, 10·4; N, 7·8. $C_{11}H_{19}ON$ requires C, 72·9; H, 10·6; N, 7·7%).

cyclo*Hexane*-cis-1 : 2-*diacetic Acid*.—A mixture of *cis*-1 : 2-biscyanomethyl*cyclo*hexane

[21] Hückel, *Annalen*, 1925, **444**, 1.

XUM

(23 g.) and 50% sulphuric acid (552 g.) was boiled under reflux for 3 hr., and then cooled. The precipitated solid on recrystallisation from aqueous methanol gave the *cis*-diacetic acid (26 g., 91·5%), m. p. 159—161° (lit.,[4] m. p. 160—161°).

Dimethyl cyclo*Hexane*-cis-1 : 2-*diacetate*.—Esterification of the above acid (26 g.), as described for the corresponding *trans*-compound, gave the cis-*dimethyl ester* (26·4 g., 90%), b. p. 91°/0·1 mm., n_D^{19} 1·4645 (Found: C, 62·7; H, 8·9. $C_{12}H_{20}O_4$ requires C, 63·1; H, 8·8%).

Hydrolysis of a sample of this ester regenerated *cyclo*hexane-*cis*-1 : 2-diacetic acid (80%), m. p. 160—161°.

2-*Hydroxymethyl*cyclo*hexylacetic Acid Lactone*.—(i) A mixture of *cis*-2-ethoxymethyl*cyclo*hexylmethyl cyanide (0·7 g.) and 50% sulphuric acid (10 g.) was boiled under reflux for 8 hr., then cooled, diluted with water, and extracted with ether. The extract was washed with aqueous sodium hydrogen carbonate and with water, and evaporated. The residue was dissolved in 10% aqueous sodium hydroxide (10 c.c.), with shaking, and the solution was washed once with ether, then acidified with sulphuric acid and extracted with ether to give an oil, which on distillation furnished 3-oxo-4-oxa*bicyclo*[4 : 4 : 0]decane (0·25 g.), b. p. 122°/4 mm., n_D^{19} 1·4915 (Found: C, 70·15; H, 9·1. Calc. for $C_9H_{14}O_2$: C, 70·1; H, 9·15%); $\nu_{max.}$ (liquid film) 1735 cm.$^{-1}$ (δ-lactone). For the *cis*-lactone, Stork and Hill [4] give b. p. 115—120°/4 mm., $\nu_{max.}$ 1727 cm.$^{-1}$.

A solution of the lactone (0·1053 g.) in ethanol (10 c.c.) was treated with 0·0900N-aqueous potassium hydroxide, added 2 c.c. at a time, phenolphthalein being used as indicator. The colour disappeared slowly after each addition and became permanent after 8 c.c. had been added. The solution was then heated (steam-bath) for a few minutes and the excess of alkali was back-titrated with 0·1095N-hydrochloric acid (0·42 c.c.) (Found: equiv., 152. Calc.: equiv., 154). The titrated solution was concentrated and mixed with a solution of *S*-benzyl*iso*thiuronium chloride (0·15 g.) in water (1 c.c.). The precipitate was recrystallised from aqueous methanol to give the S-*benzyliso*thiuronium *salt*, m. p. 140°, of 2-hydroxymethyl*cyclo*hexylacetic acid (Found: C, 60·6; H, 7·7; N, 8·3. $C_{17}H_{26}O_3N_2S$ requires C, 60·3; H, 7·7; N, 8·3%).

(ii) *trans*-2-Ethoxymethyl*cyclo*hexylmethyl cyanide (0·8 g.), on similar hydrolysis, gave a slightly impure lactone (0·35 g.), b. p. 112—116°/3 mm., n_D^{20} 1·4849 (Found: C, 69·4; H, 9·6%; equiv., determined as described above, 147), which furnished the same *S*-benzyl*iso*thiuronium salt, m. p. and mixed m. p. 139°.

Acyloin Cyclisation of Dimethyl cyclo*Hexane*-trans-1 : 2-*diacetate*.—Sodium (10·5 g.) was added in small portions with stirring during 15 min. to dry ether (1000 c.c.) and liquid ammonia (1400 c.c.), and after a further 15 min. the stirring was stopped and all air was displaced by a rapid stream of oxygen-free dry nitrogen. The nitrogen flow was then reduced, and maintained until after the final acidification stage. The *trans*-dimethyl ester (15 g.) in dry ether (1000 c.c.) was added dropwise during 8 hr. with vigorous stirring. The ammonia was allowed to evaporate at room temperature (*ca.* 24 hr.) and the flask was then warmed at 45—50° to remove the remaining ether. When the contents of the flask became dry, more dry ether (100 c.c.) was added and subsequently removed in a similar way. This process of addition and removal of ether was repeated 3 or 4 times until all the ammonia was removed. Finally, dry ether (300 c.c.) was added, followed by the gradual addition, during 20 min., of acetic acid (32 g.) in dry ether (200 c.c.). The precipitated sodium acetate was filtered off and washed with ether. The combined filtrate and washings were washed with aqueous sodium hydrogen carbonate, then with water, and were dried (Na_2SO_4) and evaporated under reduced pressure to give 3-oxo-*trans*-decalin-2α-ol (8 g., 72%), which after recrystallisation from ether–light petroleum (b. p. 40—60°) had m. p. 82—83° (Found: C, 71·9; H, 9·9. Calc. for $C_{10}H_{16}O_2$: C, 71·4; H, 9·6%); $\lambda_{max.}$ in ethanol 275 mμ (ε 28); $\nu_{max.}$ in paraffin mull 3385 (O–H stretching), 1708 (C=O stretching), 1087, 1080, 1064, 1047, 1025 cm.$^{-1}$. It readily reduced Fehling's solution, and bismuth oxide in boiling acetic acid. With aqueous 2 : 4-dinitrophenylhydrazine sulphate it immediately gave a yellow precipitate which, when heated with excess of the reagent on the steam-bath for a few minutes, gave the 2 : 4-dinitrophenylosazone of *trans*-decalin-2 : 3-dione, m. p. and mixed m. p. 219° (decomp.).

After storage for 2 months a sample of the originally pure ketol had m. p. 78—80°; it was extracted with boiling ether, and filtered from a small amount of insoluble residue. The filtrate, on concentration and dilution with light petroleum (b. p. 40—60°) gave the original ketol, m. p. 82°. The ether-insoluble material was washed several times with boiling methanol to give the dimer, trans-A/B : trans-D/E-5a : 12a-*dihydroxy*-6 : 13-*dioxaperhydropentacene*, a white powder,

XUM

m. p. 122—123° (Found: C, 71·1; H, 9·7%; *M* in camphor, 178. $C_{20}H_{32}O_4$ requires C, 71·4; H, 9·6%; *M*, 336); dissociation to the monomer is evidently almost complete in molten camphor. Infrared absorption (in paraffin mull): $\nu_{max.}$ 3413 cm.$^{-1}$ (O–H stretching) (no carbonyl band). It slowly reduced boiling Fehling's solution and bismuth oxide in boiling acetic acid. It gave no precipitate with alcoholic 2 : 4-dinitrophenylhydrazine sulphate (in which the compound was insoluble) in the cold, but on continued boiling with excess of the reagent the 2 : 4-dinitrophenylosazone of *trans*-decalin-2 : 3-dione, m. p. and mixed m. p. 219°, was formed.

A sample of crude ketol, stored for about a month, gave a much greater proportion of insoluble material, which was washed with ether to give the same dimer, m. p. and mixed m. p. 122—123°.

On one occasion, the product of the acyloin condensation, in the ethereal solution, was not washed with sodium hydrogen carbonate to free it from excess of acetic acid and the acidic ethereal solution was as such evaporated at 50° under reduced pressure; only the dimer, m. p. and mixed m. p. 122—123° (after being washed with ether) was obtained.

Derivatives of 3-*Oxo*-trans-*decalin*-2α-*ol*.—The *semicarbazone* formed prisms (from methanol), m. p. 177° (Found: C, 58·9; H, 8·15; N, 19·0. $C_{11}H_{19}O_2N_3$ requires C, 58·65; H, 8·5; N, 18·7%).

The *toluene*-p-*sulphonate*, prepared from the ketol (0·2 g.) and toluene-*p*-sulphonyl chloride (0·27 g.) in pyridine (0·6 c.c.) (12 hr. at room temperature) and isolated by precipitation with ice (yield 0·3 g.), formed needles (from methanol), m. p. 101° (Found: C, 63·5; H, 7·1; S, 9·9. $C_{17}H_{22}O_4S$ requires C, 63·3; H, 6·9; S, 9·9%).

The 3 : *5-dinitrobenzoate*, similarly prepared (yield, 72%), formed prisms (from acetone–ethanol), m. p. 147° (Found: C, 56·5; H, 5·2; N, 7·75. $C_{17}H_{18}O_7N_2$ requires C, 56·35; H, 5·0; N, 7·7%).

Reaction of the ketol (4 g.) in pyridine (13 c.c.) with acetic anhydride (5 g.) for 10 min. on the steam-bath, followed by storage at room temperature overnight, and dilution with crushed ice, gave the *acetate* (3·9 g., 77%), needles (from aqueous methanol), m. p. 64—65° (Found: C, 68·6; H, 8·7. $C_{12}H_{18}O_3$ requires C, 68·5; H, 8·6%); $\lambda_{max.}$ in ethanol 287 mμ (ε 33); $\nu_{max.}$ in carbon tetrachloride 1749 and 1733 (C=O stretching in ester and in ketone), 1233 (C–O stretching in acetate) cm.$^{-1}$.

Similar treatment of the dimeric ketol (0·22 g.) with acetic anhydride (1 g.) and pyridine (1·6 c.c.) gave the same acetate (0·21 g., 76%), m. p. and mixed m. p. 64—65°.

Reaction of the ketol acetate (0·044 g.) in methanol (1 c.c.) with 2 : 4-dinitrophenylhydrazine sulphate (0·040 g. of 2 : 4-dinitrophenylhydrazine in 0·3 c.c. of concentrated sulphuric acid and 3 c.c. of methanol) gave a precipitate which on recrystallisation from dioxan gave the *acetate* 2 : 4-*dinitrophenylhydrazone* (0·065 g., 79%) as yellow needles, m. p. 202° (Found: C, 55·1; H, 5·7; N, 13·9. $C_{18}H_{22}O_6N_4$ requires C, 55·4; H, 5·7; N, 14·35%).

Deacetylation of 3-*Oxo*-trans-*decalin*-2α-*yl Acetate*.—Treatment of the ketol acetate (0·1 g.) with methanolic sodium methoxide (*ca.* 0·01 g. of sodium in 10 c.c. of methanol) at room temperature overnight, followed by neutralisation with carbon dioxide, evaporation to dryness under reduced pressure at room temperature, and extraction of the residue with ether, regenerated the *trans*-ketol (0·055 g., 68%), which after one recrystallisation from light petroleum (b. p. 60—80°) had m. p. and mixed m. p. 82°.

Dimethylene Thioketal of 3-*Oxo*-trans-*decalin*-2α-*yl Acetate*.—A mixture of the ketol acetate (0·30 g.), ethane-1 : 2-dithiol (0·13 g.), acetic acid (3 c.c.), a small drop of sulphuric acid, and a little anhydrous sodium sulphate was kept for 24 hr. at room temperature, then diluted with ether, washed with water, then with aqueous sodium hydrogen carbonate, and again with water, and dried (Na_2SO_4). Removal of the ether afforded an oil (0·33 g., 64%) which solidified, and on recrystallisation from pentane gave the *dimethylene thioketal*, plates, m. p. 96° (Found: C, 58·7; H, 7·9; S, 22·0. $C_{14}H_{22}O_2S_2$ requires C, 58·7; H, 7·7; S, 22·4%).

Desulphurisation. A solution of the thioketal (0·25 g.) in dry ethanol (100 c.c.) was boiled under reflux with Raney nickel catalyst (10 g.) for 24 hr. The mixture was filtered and the catalyst was thoroughly washed with ethanol. The filtrate and washings were combined and evaporated to an oil (which had a strong characteristic odour of a decalinyl acetate); this was deacetylated by treatment with a catalytic amount of sodium methoxide in dry methanol (5 c.c.) under reflux for 30 min. to give a solid (0·085 g., 63%), m. p. 71—73°. One recrystallisation from light petroleum (b. p. 60—80°) gave *trans*-decalin-2α-ol, m. p. and mixed m. p. 74—75°.

XUM

Attempted Epimerisation of 3-*Oxo*-trans-*decalin*-2α-*ol*.—(i) A solution of the ketol (0·15 g.) in 1·5N-ethanolic sodium ethoxide (10 c.c.) was boiled under reflux for 10 min. Neutralisation of the cooled mixture with carbon dioxide, followed by evaporation to dryness under reduced pressure, extraction with ether, and evaporation of the dried extract, gave a residue which crystallised from light petroleum (b. p. 60—80°) to give the starting material (0·07 g.), m. p. and mixed m. p. 82—83°.

(ii) A mixture of the ketol (0·30 g.), 10% aqueous sodium hydroxide (7 c.c.), and dioxan (3 c.c.) was heated on the steam-bath for 30 min. The dioxan was removed under reduced pressure and the aqueous solution was acidified with dilute sulphuric acid. Extraction with ether again gave the starting material (0·2 g.), m. p. and mixed m. p. 82°.

Oxidation of 3-*Oxo*-trans-*decalin*-2α-*ol with Bismuth Oxide*.—The ketol (0·10 g.), bismuth trioxide (0·17 g.), and acetic acid (1·5 c.c.) were boiled under reflux for 10 min., then cooled and filtered. The filtrate was diluted with 2N-sulphuric acid and extracted with ether to give a semisolid, which when sublimed at 140°/0·3 mm. gave *trans*-decalin-2 : 3-dione (0·045 g., 46%), m. p. and mixed m. p. 98—100°; 2 : 4-dinitrophenylosazone, m. p. and mixed m. p. 219°.

Similar oxidation of the dimeric form of the above ketol (0·5 g.) with bismuth trioxide (0·7 g.) in acetic acid (5 c.c.) gave the same diketone, m. p. and mixed m. p. 99—100°.

Acyloin Cyclisation of Dimethyl cyclo*Hexane*-cis-1 : 2-*diacetate*.—The method was the same as for the corresponding *trans*-compound. The *cis*-ester (4 g.) gave on evaporation of the washed ethereal solution a paste which was dissolved in hot light petroleum (b. p. 60—80°) and cooled; the solid which crystallised out was collected, and the mother-liquor was preserved. Recrystallisation of the solid from ether–light petroleum (b. p. 40—60°) gave 3-oxo-*cis*-decalin-2α-ol (0·8 g., 27%), m. p. 89—90° (Found: C, 71·0; H, 9·6. Calc. for $C_{10}H_{16}O_2$: C, 71·4; H, 9·6%); a mixed m. p. with the *trans*-isomer, m. p. 82°, was 59° (reported [2] m. p. for one of the two possible ketols: 88—90°); $\lambda_{max.}$ in ethanol 273 mμ (ε 23); $\nu_{max.}$ in paraffin mull, 3425 (O–H stretching), 1709 (C=O stretching), 1089, 1080, 1047, 1040, 1010 cm.$^{-1}$. It readily reduced Fehling's solution, and with excess of aqueous 2 : 4-dinitrophenylhydrazine sulphate it gave the 2 : 4-*dinitrophenylosazone* of *cis*-decalin-2 : 3-dione, red needles (from chloroform–methanol), m. p. 226—227° (Found: C, 50·2; H, 4·3; N, 20·8. $C_{22}H_{22}O_8N_8$ requires C, 50·2; H, 4·2; N, 21·3%).

Unlike the *trans*-analogue, 3-oxo-*cis*-decalin-2α-ol was unchanged after storage for several months.

The light petroleum mother-liquors spontaneously evaporated to dryness in 14 days, and the residue was boiled with ether to give an ether-insoluble solid (soluble in hot methanol) which was a *cis*-dimer, cis-A/B : cis-D/E-5a : 12a-*dihydroxy*-6 : 13-*dioxaperhydropentacene* (0·32 g.), m. p. 110—112° (Found: C, 71·1; H, 9·7. $C_{20}H_{32}O_4$ requires C, 71·4; H, 9·6%); $\nu_{max.}$ in paraffin mull 3552 and 3437 (O–H stretching) cm.$^{-1}$.

Concentration of the ethereal solution and crystallisation of the residue from ether gave *cis*-decalin-2α : 3β-diol (0·06 g.), m. p. and mixed m. p. 125° (Found: C, 70·3; H, 10·7. Calc. for $C_{10}H_{18}O_2$: C, 70·5; H, 10·65%) (for proof of configuration see following paper).

Derivatives of 3-*Oxo*-cis-*decalin*-2α-*ol*.—The *semicarbazone*, needles (from methanol), m. p. 195—196° (Found: C, 58·5; H, 8·55; N, 18·3%), the *toluene*-p-*sulphonate*, needles (from methanol), m. p. 109° (Found: C, 63·2; H, 7·2; S, 9·8%), the *acetate*, needles (from aqueous methanol), m. p. 74—75° (Found: C, 68·6; H, 8·8%), and the *acetate* 2 : 4-*dinitrophenylhydrazone*, yellow needles (from ethyl acetate–methanol), m. p. 203—204° (Found: C, 55·3; H, 5·8; N, 14·3%), were all prepared as described for the corresponding *trans*-derivatives. Light absorption of the acetate: $\lambda_{max.}$ in ethanol 282 mμ (ε 25); $\nu_{max.}$ in carbon tetrachloride 1752 and 1732 (C=O stretching in ester and in ketone), 1227 (C–O stretching in acetate) cm.$^{-1}$.

Dimethylene Thioketal of 3-*Oxo*-cis-*decalin*-2α-*yl Acetate*.—Prepared from the acetate (0·66 g.) by the same procedure as for the *trans*-decalin analogue, the *dimethylene thioketal* crystallised from pentane in prisms (0·70 g., 77%), m. p. 84—85° (Found: C, 58·9; H, 7·9; S, 22·6. $C_{14}H_{22}O_2S_2$ requires C, 58·7; H, 7·7; S, 22·4%).

Desulphurisation. The thioketal (0·64 g.), Raney nickel catalyst (W6) (10 g.), and dry ethanol (100 c.c.) were boiled under reflux for 24 hr. The product was isolated and deacetylated as described for the *trans*-isomer to give *cis*-decalin-2α-ol, m. p. 100—102°; the m. p. of a mixture with an authentic sample (m. p. 104°) was 100—102°.

3-*Oxo*-cis-*decalin*-2β-*yl Acetate*.—A mixture of the dimeric *cis*-ketol (m. p. 110—112°; 0·47 g.), acetic anhydride (2·5 c.c.), and pyridine (3·6 c.c.) was heated on the steam-bath for

10 min. The mixture was kept for 18 hr. at room temperature and was then diluted with ice-water. The solid was recrystallised from aqueous methanol to give 3-*oxo*-cis-*decalin*-2β-*yl acetate* (0·46 g., 79%), needles, m. p. 98—99° (Found: C, 68·5; H, 8·8. $C_{12}H_{18}O_3$ requires C, 68·5; H, 8·6%); $\lambda_{max.}$ in ethanol 282 mμ (ε 27); $\nu_{max.}$ in carbon tetrachloride 1750 and 1733 (C=O stretching in ester and ketone), 1231 and 1223 (C–O stretching in acetate) cm.$^{-1}$.

This ketol acetate (0·028 g.) with 2 : 4-dinitrophenylhydrazine sulphate in methanolic sulphuric acid gave a solid which on recrystallisation from dioxan–methanol (1 : 2) gave the 2 : 4-*dinitrophenylhydrazone* of 3-oxo-*cis*-decalin-2β-yl acetate (0·036 g., 69%), yellow needles, m. p. 217—218° (Found: C, 55·4; H, 5·7; N, 14·3. $C_{18}H_{22}O_6N_4$ requires C, 55·4; H, 5·7; N, 14·35%). The m. p. of a mixture with the 2 : 4-dinitrophenylhydrazone of 3-oxo-*cis*-decalin-2α-yl acetate was 195°.

Deacetylation of the Acetates of 3-*Oxo*-cis-*decalin*-2α- *and* -2β-*ol.*—(i) The 2α-acetate (0·062 g.) was treated with methanolic sodium methoxide (*ca.* 0·003 g. in 10 c.c. of methanol) for 18 hr. at room temperature. The solution was then neutralised with carbon dioxide and evaporated to dryness under reduced pressure. The residue was stirred with a little water and extracted with ether. Removal of the solvent from the dried extract and crystallisation of the residue from light petroleum (b. p. 60—80°) gave 3-oxo-*cis*-decalin-2α-ol, m. p. and mixed m. p. 88—89°.

(ii) Exactly similar treatment of the 2β-acetate (0·060 g.) also gave 3-oxo-*cis*-decalin-2α-ol, m. p. and mixed m. p. 89—90°.

Formation of cis-*Decalin*-2 : 3-*dione* 2 : 4-*Dinitrophenylosazone from the Acetates of* 3-*Oxo*-cis-*decalin*-2α- *and* -2β-*ol.*—(i) The 2α-acetate (0·02 g.) in methanol (1 c.c.) was treated with *ca.* 5 mol. of methanolic 2 : 4-dinitrophenylhydrazine sulphate. The mixture was heated on the steam-bath whereupon the yellow precipitate quickly turned orange-red. The heating was continued for 1 hr. and then the precipitate was collected, washed with methanol, and crystallised from chloroform–methanol, to give *cis*-decalin-2 : 3-dione 2 : 4-dinitrophenylosazone (0·04 g.), m. p. and mixed m. p. 226—227°.

(ii) Similar treatment of the 2β-acetate (0·02 g.) gave the same 2 : 4-dinitrophenylosazone (0·04 g.), m. p. and mixed m. p. 226—227°.

The work described in this and the following paper was carried out during the tenure (by M. E. A.) of a Foreign Scholarship awarded by the Government of Pakistan.

Department of Organic Chemistry, Imperial College of Science and Technology, South Kensington, London, S.W.7. [*Received, December 5th,* 1957.]

---

435. *Alicyclic Glycols. Part XVII.*[1] *The Decalin*-2 : 3-*diols.*

By Md. Erfan Ali and L. N. Owen.

Confusion over the identity, individuality, and configuration of certain *trans*-decalin-2 : 3-diols has been resolved by a re-investigation of earlier claims and by the synthesis of the three possible stereoisomers; the three *cis*-decalin-2 : 3-diols have also been synthesised. The configurations of the six diols are established by relation to the ketols described in the preceding paper. The degrees of hydrogen-bonding, as shown by the infrared spectra of the diols, and the rates of oxidation by lead tetra-acetate, are in accord with the conformations compatible with the assigned configurations.

There are six possible racemic or *meso*-forms of decalin-2 : 3-diol. In the *cis*-fused system, one *trans*- (2α : 3β ≡ 2β : 3α)* and two *cis*-diols (2α : 3α and 2β : 3β) are capable of existence, but none has been described. In the *trans*-decalin configuration, there are two *trans*-diols (2α : 3β and 2β : 3α) and one *cis* (2α : 3α = 2β : 3β); the preparation of these has been studied by several investigators, but the results are conflicting in many respects.

* *cis*-Decalin-2α : 3β- and -2β : 3α-diols are enantiomorphs, but as the present paper is concerned only with *meso* or racemic forms they are in effect identical.

[1] Part XVI, preceding paper.

Leroux [2] obtained a diol, m. p. 160°, (i) by alkaline hydrolysis of a 2 : 3-dibromo-*trans*-decalin, (ii) by acidic or alkaline hydrolysis of 2 : 3-epoxy-*trans*-decalin (IV), and (iii) from the corresponding iodohydrin. On the incorrect assumption that epoxides undergo *cis*-fission, the diol was assigned a *cis*-configuration. By reaction of the same dibromide with silver acetate, and hydrolysis of the product, he obtained a diol, m. p. 141° (erroneously assigned a *trans*-configuration), and a molecular compound, m. p. 125°, which he showed to be composed of equimolecular amounts of the two diols, m. p.s 160° and 141°, not separable by fractional crystallisation. The positions of the hydroxyl groups in all these products were established by oxidation to *cyclo*hexane-*trans*-1 : 2-diacetic acid. Hückel and Naab [3] confirmed these observations but found that the diol, m. p. 141°, gave an *iso*propylidene derivative from which it could be regenerated, and they therefore corrected the earlier configurational assignments, at the same time pointing out that the higher-melting isomer (for which they gave m. p. 163°) must be one of the two possible *trans*-diols. Lehmann and Krätschell,[4] by treatment of 3-chloro-2-oxo-*trans*-decalin with boiling 40% sodium hydroxide obtained a diol, m. p. 168°, which they suggested was formed by disproportionation of the initially-formed ketol; its structure was confirmed by oxidation to *cyclo*hexane-*trans*-1 : 2-diacetic acid, but it was not compared with the diol, m. p. 163°, described by the earlier workers.

The later work of Ganapathi,[5,6] which, as will be shown, included a number of erroneous observations and incorrect interpretations, confused the situation. He reported the formation of three diols, m. p.s 166°, 128—129°, and 141°, by reduction of *trans*-decalin-2 : 3-dione (V) under various conditions. The first of these he considered to be identical with Leroux's diol, m. p. 160°, *and* with Lehmann and Krätschell's diol, m. p. 168°, and in a repetition of Leroux's experiments claimed that the diol obtained either from the dibromide or from the epoxide had m. p. 166°; he did not quote a mixed m. p. with his own product from the diketone. He also considered his diol, m. p. 128—129°, to be identical with Leroux's product of m. p. 125°, and yet to be a single stereoisomer, to which he assigned a *cis*-configuration. Other claims were that none of the diols reacted with acetone, and that his compound, m. p. 128—129°, was quantitatively isomerised by acetone–sulphuric acid into that of m. p. 166°. His fallacious arguments [6] for allocations of configuration need not be considered, as they are based on the assumption that there are one *trans*- and two *cis*-diols.

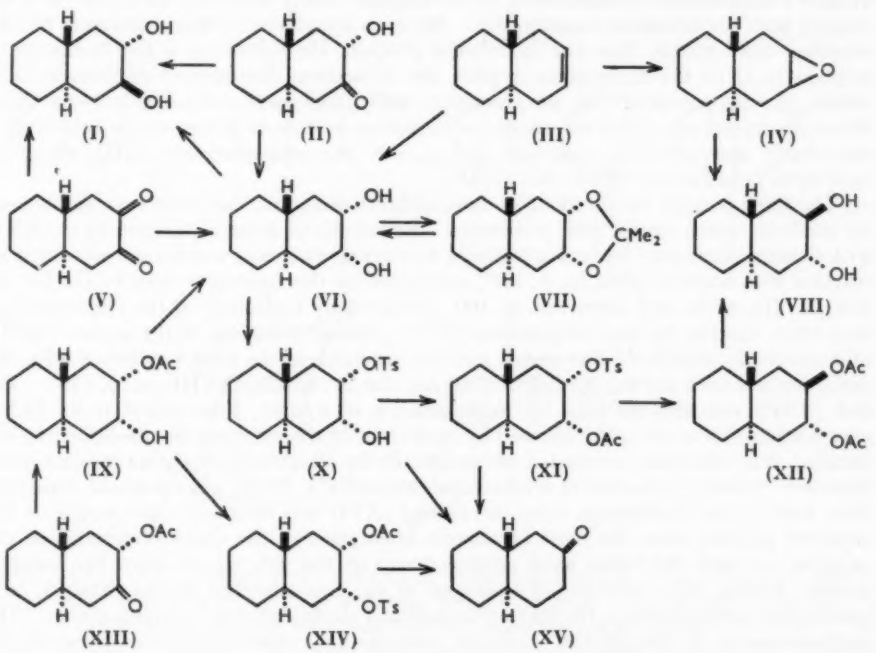
Other incidental references have been made to the *cis*-diol, m. p. 141°,[4,7,8] and the *trans*-diol, m. p. 163°,[8] but no suggestion has been made as to the precise configuration of the latter.

We began our investigation with a re-examination of some of Ganapathi's experiments. Reduction of the diketone (V) with aluminium amalgam in moist ether, aqueous ethanol, or dry ethanol gave in good yield a product, m. p. 128—129°, unaltered by fractional crystallisation; it was thus either an individual stereoisomer, as claimed by Ganapathi, or a molecular compound. On treatment with acetone–sulphuric acid it gave, in almost equal yields, a diol, m. p. 168°, and the *iso*propylidene derivative (VII) of *trans*-decalin-2α : 3α-diol; hydrolysis of the derivative furnished the *cis*-diol (VI), m. p. 141°. By mixing equal amounts of the two diols the original material, m. p. 128—129°, was regenerated; the latter is therefore unquestionably a molecular compound. Ganapathi's reported [6] quantitative isomerisation of his diol, m. p. 128—129°, into one of m. p. 166° can thus be attributed to inaccurate quantitative experimentation coupled with a failure

[2] Leroux, *Ann. Chim.* (*France*), 1910, **21**, 458.
[3] Hückel and Naab, *Annalen*, 1933, **502**, 136.
[4] Lehmann and Krätschell, *Ber.*, 1935, **68**, 360.
[5] Ganapathi, *J. Indian Chem. Soc.*, 1938, **15**, 407.
[6] *Idem*, *Ber.*, 1939, **72**, 1381.
[7] Lehmann and Krätschell, *Ber.*, 1934, **67**, 1857; Burnop, Elliott, and Linstead, *J.*, 1940, 720; Cosciug, *Ann. Sci. Univ. Jassy*, 1941, I, **27**, 303, 320; Mousseron and Granger, *Bull. Soc. chim. France*, 1943, **10**, 42.
[8] Criegee, Büchner, and Walther, *Ber.*, 1940, **73**, 571.

to detect any *iso*propylidene derivative. It is also untrue that the diol, m. p. 168° (166°), from the diketone is identical with that obtained from 2 : 3-epoxy-*trans*-decalin (IV); we find that the epoxide gives a diol, m. p. 163°, as stated by Hückel and Naab,[3] and that there is a large depression of melting point on admixture with the diol, m. p. 168°. These must therefore be the two possible *trans*-diols. Contrary to Ganapathi,[6] it follows that the molecular compound, m. p. 128—129° (141° + 168°), is *not* identical with that of m. p. 125° (141° + 163°); this again is immediately evident from a determination of mixed melting point.

It is now recognised [9,10] that hydration of an epoxy*cyclo*hexane normally leads to a diaxial diol. Consequently the compound, m. p. 163°, should be the 2β : 3α-diol (VIII), and the isomer, m. p. 168°, the 2α : 3β-diol (I); it is understandable that the latter, with



the more stable diequatorial conformation, should be the product formed under the drastic alkaline conditions used by Lehmann and Krätschell.[4]

The availability of 3-oxo-*trans*-decalin-2α-ol (II), of established [1] configuration, enabled us to confirm these deductions. Reduction of the ketol with aluminium amalgam, sodium amalgam, or lithium aluminium hydride and also reduction of the dimeric ketol with lithium aluminium hydride gave in each case the molecular compound, m. p. 128—129°, from which the two constituent diols (I) and (VI) were again isolated by the process already described; the α-configuration at $C_{(2)}$ in the ketol (II) clearly demands the allocation of the 2α : 3β-configuration (I) to the *trans*-diol so produced. Catalytic hydrogenation of the ketol, and of its dimer,[1] over platinum in acetic acid, gave the 2α : 3α-diol (VI) as the main product, in agreement with the expectation [9] that under these conditions the reduction would proceed with preferential formation of an axial hydroxyl group. This stereospecific

[9] Barton, *J.*, 1953, 1027.
[10] Fürst and Scotoni, *Helv. Chim. Acta*, 1953, **36**, 1332, 1410; Schmidlin and Wettstein, *ibid.*, p. 1241.

reduction was even more clearly illustrated by hydrogenation of the ketol acetate (XIII), which gave an almost quantitative yield of the monoacetate (IX) of the 2α : 3α-diol. A more convenient preparative route to the latter diol, however, was the *cis*-hydroxylation of *trans*-Δ^2-octalin (III), by Woodward's method,[11] with iodine and silver acetate in aqueous acetic acid. Toluene-*p*-sulphonation of the axial hydroxyl group in the 2α-monoacetate (IX) was slow, but afforded the 2α-acetate 3α-toluene-*p*-sulphonate (XIV), which with alkali showed behaviour typical[12] of a monotoluene-*p*-sulphonate of a *cis*-diol and gave *trans*-decalin-2-one (XV).

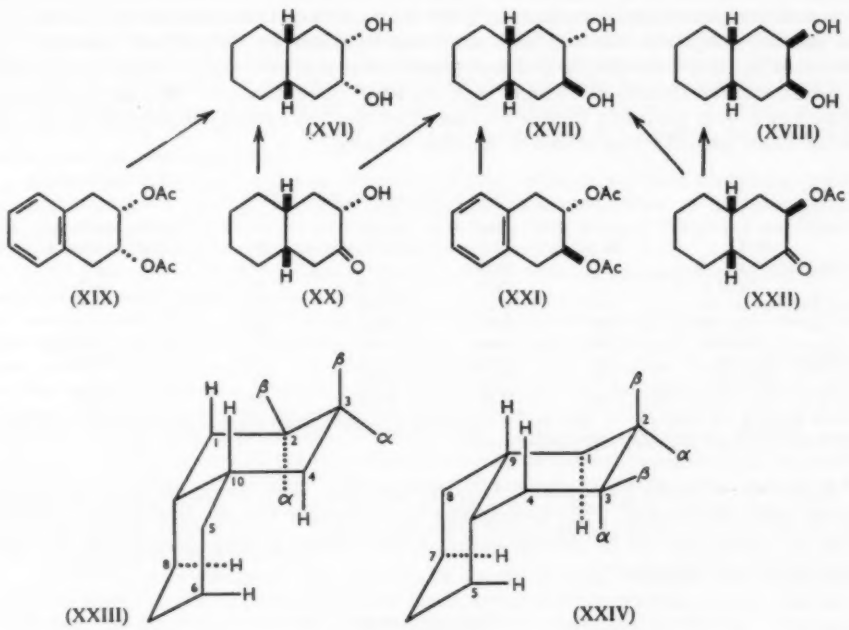
Epimerisation of the 2α : 3α-diol with sodium ethoxide gave the diequatorial 2α : 3β-isomer, whilst conversion into the diaxial 2β : 3α-diol was effected as follows. Reaction of the 2α : 3α-diol with one mol. of toluene-*p*-sulphonyl chloride in pyridine gave an excellent yield of a monotoluene-*p*-sulphonate, which was only slowly converted by an excess of the reagent into the ditoluene-*p*-sulphonate. Since an equatorial hydroxyl group is usually esterified more readily than one in an axial position, the monoester is the 2α-toluene-*p*-sulphonate (X). On acetylation it gave the 3α-acetate 2α-toluene-*p*-sulphonate (XI), which, like its precursor (X), on treatment with alkali gave *trans*-decalin-2-one (XV). When the mixed ester (XI) was treated with sodium acetate in boiling acetic anhydride it was slowly converted, by inversion at $C_{(2)}$, into the *trans*-diacetate (XII), which on hydrolysis furnished the 2β : 3α-diol (VIII).

The three possible *cis*-decalin-2 : 3-diols, hitherto unknown, have also been synthesised by methods which prove their structures. Reduction of 3-oxo-*cis*-decalin-2α-ol (XX)[1] with lithium aluminium hydride afforded a mixture of two diols which were separated by reaction with acetone; that, m. p. 125°, unaffected by this treatment must be the 2α : 3β-diol (XVII), whilst the isomer, m. p. 100°, obtained by hydrolysis of the *iso*propylidene derivative, has the 2α : 3α-configuration (XVI). Similar reduction of the acetate (XXII) of 3-oxo-*cis*-decalin-2β-ol[1] also gave a mixture, separable in the same way into the 2β : 3α-diol [identical with the 2α : 3β-diol (XVII)] and the 2β : 3β-diol (XVIII), m. p. 118°. The diol (XVII) was also obtained by hydrogenation of *trans*-2 : 3-diacetoxytetralin (XXI) over platinum in acetic acid, followed by hydrolysis of the resulting 2α : 3β-diacetoxy-*cis*-decalin; this reduction occurred stereospecifically by *cis*-addition, no other product being detected. Similar reduction of *cis*-2 : 3-diacetoxytetralin (XIX) gave a mixed diacetate, from which, after hydrolysis, some 2α : 3α-diol (XVI) was obtained; this would be the expected product from the most favourable orientation of the diacetoxytetralin on the catalyst, *i.e.* with the bulky axial acetoxy-group on the side remote from the catalyst surface, leading, after addition of hydrogen to the side adsorbed on the catalyst, to a *trans*-configuration between the acetoxy-groups and the bridgehead hydrogen atoms. The nonhomogeneity of the product, however, indicates that other orientations occur on the catalyst; probably some 2β : 3β-diacetoxy-*cis*-decalin was also formed, and the possibility of some *trans*-addition cannot be excluded. Some experiments were also carried out on the hydrogenation, over platinum, of naphthalene-2 : 3-diol, but as the main product formed under mild conditions was the molecular compound of tetralin-*cis*- and -*trans*-2 : 3-diol it was evident that complete hydrogenation would lead to a mixture, and this approach was therefore not pursued.

The infrared absorption maxima of the diols in the 3000 $cm.^{-1}$ region (in dilute carbon tetrachloride solution), and the rates of oxidation by lead tetra-acetate are given in the Table, which also includes, for comparison, the corresponding data for the two *cyclo*hexane-1 : 2-diols. The frequency difference, Δν, between the maxima for the bonded and the unbonded hydroxyl groups is a measure of the strength of the intramolecular hydrogen bonding,[13,14] and the figures for the *trans*-decalin-2α : 3α- and the -2α : 3β-diol are in good

[11] Cf. Ginsburg, *J. Amer. Chem. Soc.*, 1953, **75**, 5746.
[12] Clarke and Owen, *J.*, 1949, 315; Owen and Saharia, *J.*, 1953, 2582.
[13] Kuhn, *J. Amer. Chem. Soc.*, 1952, **74**, 2492.
[14] *Idem*, *ibid.*, 1954, **76**, 4323.

agreement with those for the *cyclo*hexanediols of corresponding configuration; the diaxial *trans*-decalin-2β : 3α-diol, as expected, showed no hydrogen bonding. In the *cis*-decalin series the greater degree of bonding in the 2α : 3α-diol is explicable if inter-ring repulsions [15] are considered, because in each possible double-chair form (XXIII) and (XXIV) there is a strong non-bonded interaction between one hydroxyl group and an axial hydrogen atom in the other ring, *viz.* $O_{(2)}$–$H_{(8)}$ and $O_{(3)}$–$H_{(5)}$, respectively; steric strain is thus the same in both conformations * and can only be relieved by displacement of the axial hydroxyl



group, at $C_{(2)}$ or $C_{(3)}$, respectively, towards its equatorial position, thus bringing it nearer to the other hydroxyl group. By applying Kuhn's findings,[13] a frequency difference of 45 cm.$^{-1}$ can be accounted for by a reduction in projection angle (between the two C–OH bonds, viewed along the $C_{(2)}$–$C_{(3)}$ axis) from the normal value of 60° to one of 40°. A scale model shows that such a distortion can be brought about without undue strain, and that it increases the $O_{(2)}$–$H_{(8)}$ or $O_{(3)}$–$H_{(5)}$ distance from 1·7 Å to 2·2 Å. *cis*-Decalin-2α : 3β-diol will clearly exist preferentially in the particular double-chain form (XXIV) in which the hydroxyl groups are in diequatorial rather than diaxial positions; consequently, non-bonded interaction between $O_{(2)}$ and $H_{(8)}$ does not arise, and Δν is not enlarged. In the 2β : 3β-diol there is neither $O_{(2)}$–$H_{(8)}$ nor $O_{(3)}$–$H_{(5)}$ interaction in either of the forms (XXIII) or (XXIV).

The rates of oxidation of *trans*-decalin-2α : 3α- and -2α : 3β-diol were practically identical with those of the corresponding *cyclo*hexane-1 : 2-diol. For the *trans*-diols this is not surprising, but the similarity between the *cis*-diols is interesting because the two C–OH bonds in *trans*-decalin-2α : 3α-diol, unlike those in *cyclo*hexane-*cis*-1 : 2-diol, cannot become coplanar even if the ring is in a boat form. This is because coplanarity of the C–OH bonds in the 2α : 3α-diol requires coplanarity of $C_{(1)}$, $C_{(2)}$, $C_{(3)}$, and $C_{(4)}$, *i.e.* a boat form with sides

* These are mirror images for the 2α : 3α- and also for the 2β : 3β-, but not for the 2α : 3β-diol.

[13] Cf. Mills, *J.*, 1953, 260; Dauben, Tweit, and Mannerskantz, *J. Amer. Chem. Soc.*, 1954, **76**, 4420.

2, 3, 9, and 10, but owing to the *trans*-junction of the rings only boat forms with sides 1, 9, 3, and 4, or 1, 2, 4, and 10, are possible; the coplanar arrangement is momentarily attained in passing from the chair to either of the boats, but the conformation is highly unfavourable. It seems unlikely, therefore, from the similarity in rates, that the oxidation of *cyclo*hexane-*cis*-1 : 2-diol with lead tetra-acetate can involve a *planar* cyclic intermediate, though both with this diol and with *trans*-decalin-2α : 3α-diol there may be some small displacement towards such a state. The comparatively slow rate of oxidation of the diaxial *trans*-decalin-2β : 3α-diol is in accordance with expectation, there being no anomaly such as that reported by Djerassi *et al.*,[16] who found with certain *allo*steroid-2 : 3-diols that the diaxial compound was oxidised more rapidly than its diequatorial isomer. The behaviour of *cis*-decalin-2α : 3β-diol was almost identical with that of *cyclo*hexane-*trans*-1 : 2-diol, but *cis*-decalin-2α : 3α-diol was oxidised three times as fast as *cyclo*hexane-*cis*-1 : 2-diol, thus providing further evidence that the two hydroxyl groups in the 2α : 3α-diol are closer together than in any of the other isomers.

Diol	M. p.	Infrared absorption max. ($cm.^{-1}$) Free OH	Bonded OH	$\Delta\nu$	Oxidn. rate constant ($mole^{-1}$ l. $min.^{-1}$; 25°)
*cyclo*Hexane-*cis*-1 : 2-	—	3626	3587	39 *	8·1 †
,, *trans*-1 : 2- ...	—	3634	3602	32 *	0·33 ‡
trans-Decalin-2α : 3α-	141°	3625	3588	37	8·1 §
,, 2α : 3β-	168	3630	3600	30	0·37
,, 2β: 3α-	163	3630	—	0	0·028 §
cis-Decalin-2α : 3α-	100	3632	3587	45	24·0
,, 2β : 3β-	118	3625	3592	33	—
,, 2α : 3β-	125	3627	3597	30	0·29

* Ref. 13. † Ref. 17. ‡ Ref. 18. § Criegee *et al.*[8] give 4·6 and 0·021 at 20° for two *trans*-decalin-2 : 3-diols, m. p.s 141° and 163°, respectively.

Rates of oxidation by sodium metaperiodate, also, were measured for *trans*-decalin-2α : 3β- and -2β : 3α-diol. The bimolecular rate constant for the diequatorial diol was about ten times that for the diaxial isomer, a ratio similar to that observed for the oxidations with lead tetra-acetate.

Experimental

trans-*Decalin-2-one* 2 : 4-*dinitrophenylhydrazone*, prepared from the ketone in the usual way, formed yellow needles (from ethyl acetate), m. p. 174° (Found: C, 57·6; H, 6·1; N, 16·9. $C_{16}H_{20}O_4N_4$ requires C, 57·8; H, 6·1; N, 16·9%).

Reduction of trans-*Decalin-2 : 3-dione.*—(i) *In moist ether.* Following Ganapathi's method,[5] treatment of the diketone (0·35 g.) with aluminium amalgam (1·5 g.) in ether (150 c.c.) saturated with water gave a product which was recrystallised from light petroleum (b. p. 80—100°) to give the *molecular compound*, m. p. 128—129°, of *trans*-decalin-2α : 3α-diol and *trans*-decalin-2α : 3β-diol (0·28 g., 78%) (Found: C, 70·7; H, 10·8. $2C_{10}H_{18}O_2$ requires C, 70·5; H, 10·65%). Ganapathi [5] gave m. p. 126° for his product, considered to be a single stereoisomer.

(ii) *In aqueous ethanol.* A solution of the diketone (0·31 g.) in ethanol (50 c.c.) was added to aluminium amalgam (1 g.). Water was occasionally added to maintain a steady reaction, which was complete in 8 hr. The aluminium hydroxide was filtered off and washed with ethanol, and the combined filtrate and washings were evaporated to a crystalline residue, which on recrystallisation from light petroleum (b. p. 80—100°) gave the same molecular compound (0·20 g., 62%), m. p. and mixed m. p. 126—128°. Fractional crystallisation from benzene did not separate the components.

(iii) *In dry ethanol.* A mixture of the diketone (0·15 g.), aluminium amalgam (0·5 g.), and dry ethanol (25 c.c.) was stirred and heated at 70° until (6 hr.) all the amalgam had reacted.

[16] Djerassi and Ehrlich, *J. Org. Chem.*, 1954, **19**, 1351; cf. Djerassi, Grossnickle, and High, *J. Amer. Chem. Soc.*, 1956, **78**, 3166, footnote 58.
[17] Eliel and Pillar, *J. Amer. Chem. Soc.*, 1955, **77**, 3600.
[18] Ali and Owen, *J.*, 1958, 1066.

The mixture was then diluted with water, filtered, and worked up; it gave the same molecular compound, m. p. and mixed m. p. 128—129°.

Separation of the Molecular Compound of trans-*Decalin-2α : 3α- and -2α : 3β-diol by Reaction with Acetone.*—The molecular compound (0·40 g.) in dry acetone (30 c.c.) containing sulphuric acid (0·1 g.) was kept for 24 hr. at room temperature. The solution was then made faintly alkaline with concentrated ammonia and the precipitated ammonium sulphate was filtered off. Evaporation of the filtrate gave an oil, which was dissolved in hot light petroleum (b. p. 80—100°) (2 c.c.). When this was cooled in ice a solid crystallised, which was recrystallised from benzene, giving trans-*decalin-2α : 3β-diol* (0·18 g., 45%), needles, m. p. 168° (Found: C, 70·4; H, 10·7. $C_{10}H_{18}O_2$ requires C, 70·5; H, 10·65%); infrared absorption: see Table. The mother liquor was evaporated and the residue was again treated with light petroleum (b. p. 40—60°) (1 c.c.) and cooled in ice to give a small amount of the same diol, m. p. 166°. The oil obtained by evaporation of the solution was distilled to give 2α : 3α-iso*propylidenedioxy*-trans-*decalin* (0·22 g., 44%), b. p. 90°/16 mm., n_D^{20} 1·4728 (Found: C, 74·1; H, 10·7. $C_{13}H_{22}O_2$ requires C, 74·2; H, 10·5%); Hückel and Naab [3] reported its formation, but recorded no analysis or physical constants.

Hydrolysis of the *iso*propylidene compound (0·22 g.) with 2N-sulphuric acid (2 c.c.) for 2 hr. on the steam-bath, followed by extraction with ether and evaporation of the dried (Na_2SO_4) extract, gave a solid which after two recrystallisations from benzene furnished *trans*-decalin-2α : 3α-diol (0·14 g.), m. p. 141°; infrared absorption: see Table.

A 1 : 1 mixture of the 2α : 3β- and 2α : 3α-diol, dissolved in benzene and evaporated, gave the original molecular compound, m. p. 128—129°.

trans-*Decalin-2β : 3α-diol.*—Prepared by Hückel and Naab's method [3] from 2 : 3-epoxy-*trans*-decalin, this had m. p. 163°; infrared absorption: see Table. A mixture with the 2α : 3β-diol (m. p. 168°) had m. p. *ca.* 130°. Equal amounts of the 2β : 3α- and the 2α : 3α-diol were dissolved in hot benzene; on cooling, the molecular compound, m. p. 125°, was deposited. A mixture of this with the 2α : 3β- and 2α : 3α-molecular compound (m. p. 128—129°) had m. p. 110—115°.

Reduction of 3-*Oxo*-trans-*decalin-2α-ol.*—(i) *With aluminium amalgam in aqueous ethanol.* The ketol (0·15 g.) in ethanol (50 c.c.) was reduced with aluminium amalgam (1 g.) as described above for *trans*-decalin-2 : 3-dione. The product crystallised from light petroleum (b. p. 80—90°) to give the molecular compound, m. p. and mixed m. p. 128—129°, of *trans*-decalin-2α : 3α- and -2α : 3β-diol (0·08 g., 53%). The product was separated into its constituents by reaction with acetone, as described above.

(ii) *With sodium amalgam.* The ketol (0·14 g.), 3% sodium amalgam (2·5 g.), methanol (15 c.c.), and water (2 c.c.) were stirred until the evolution of hydrogen had ceased. The alcohol layer was then neutralised with 2N-hydrochloric acid and evaporated to dryness. The residue was extracted with ether to yield a product which on recrystallisation from benzene gave the above molecular compound (0·11 g., 78%), m. p. and mixed m. p. 129—130°.

(iii) *With lithium aluminium hydride.* The ketol (0·15 g.) in dry ether (10 c.c.) was added to a stirred solution of lithium aluminium hydride (0·30 g.) in dry ether (15 c.c.). After an hour, an excess of dilute sulphuric acid was added, and the ether layer was removed; the aqueous portion was extracted with ether, and the combined ethereal solutions were evaporated to a crystalline residue, m. p. 122—126°. Two recrystallisations from light petroleum (b. p. 80—90°) gave the same molecular compound (0·146 g., 96%), m. p. and mixed m. p. 128—130°.

(iv) *By catalytic hydrogenation.* The ketol (0·15 g.) in acetic acid (10 c.c.) was hydrogenated over platinum oxide (0·03 g.) at 19° and 760 mm.; 22 c.c. of hydrogen were absorbed (calc. 21·4 c.c.) during 3 hr. Removal of the catalyst followed by evaporation of the solvent under reduced pressure gave an oil which was diluted with water and extracted with ether. The extract was washed with aqueous sodium hydrogen carbonate, dried (Na_2SO_4), and concentrated to a solid (0·145 g.), m. p. 133—135°. This was fractionally crystallised five times from benzene to give *trans*-decalin-2α : 3α-diol (0·048 g., 31·5%), m. p. and mixed m. p. 140—141°, as the less soluble portion, and the molecular compound of *trans*-decalin-2α : 3α- and -2α : 3β-diol (*ca.* 6 mg., 4%), m. p. and mixed m. p. 128—129°, from the more soluble fractions.

Reduction of trans-A/B : trans-D/E-5a : 12a-*Dihydroxy*-6 : 13-*dioxaperhydropentacene.*—(i) *With lithium aluminium hydride.* Because of the very low solubility of the dimer [1] in ether, this reduction was effected in a Soxhlet extraction apparatus, with the dimer (0·2 g.) in the thimble and a solution of lithium aluminium hydride (0·2 g.) in dry ether (100 c.c.) in the flask. Refluxing was maintained for 2 days, during which most of the dimer disappeared. The mixture was

then diluted with sulphuric acid, and the product isolated as usual to give the molecular compound, m. p. and mixed m. p. 128—129°.

(ii) *By catalytic hydrogenation.* Hydrogenation of a suspension of the dimer (0·078 g.) in acetic acid (10 c.c.) over platinum oxide (0·03 g.) during 14 hr., followed by working up as before and one crystallisation from benzene, furnished *trans*-decalin-2α : 3α-diol, m. p. and mixed m. p. 139—140°.

Hydrogenation of 2α-*Acetoxy*-3-*oxo*-trans-*decalin*.—The acetate [1] (3·8 g.) in acetic acid (100 c.c.) was hydrogenated at 19° and 760 mm. over platinum oxide (0·2 g.); 453 c.c. of hydrogen were taken up during 7 hr. (calc., 433 c.c.). The filtered solution was concentrated under reduced pressure, diluted with water, and extracted with ether. The extract was washed with aqueous sodium hydrogen carbonate and with water, and evaporated to a solid (3·8 g.), m. p. 79—82°, which on recrystallisation from light petroleum (b. p. 40—60°) gave trans-*decalin*-2α : 3α-*diol* 2-*monoacetate*, needles, m. p. 83° (Found: C, 67·5; H, 9·5. $C_{12}H_{20}O_3$ requires C, 67·9; H, 9·5%).

Treatment of this monoacetate (0·10 g.) with a trace of sodium methoxide in dry methanol (8 c.c.) for 30 min. under reflux, followed by isolation of the product as usual, gave *trans*-decalin-2α : 3α-diol (0·08 g.), m. p. and mixed m. p. 141°.

trans-*Decalin*-2α : 3α-*diol* 2-*Acetate* 3-*Toluene*-p-*sulphonate*.—The above 2-monoacetate (0·13 g.) was treated with toluene-*p*-sulphonyl chloride (0·13 g.) in pyridine (1·5 c.c.) at room temperature overnight. Dilution with water gave unchanged monoacetate, m. p. and mixed m. p. 81—82°. This was again treated with toluene-*p*-sulphonyl chloride (0·13 g.) in pyridine (0·5 c.c.) at room temperature for 96 hr. Dilution with crushed ice gave a solid which was recrystallised from methanol, giving trans-*decalin*-2α : 3α-*diol* 2-*acetate* 3-*toluene*-p-*sulphonate* (0·09 g., 41%), needles, m. p. 106—107° (Found: C, 62·2; H, 7·2; S, 8·7. $C_{19}H_{26}O_5S$ requires C, 62·3; H, 7·15; S, 8·75%).

Treatment of this mixed ester (0·014 g.) with 2N-methanolic sodium methoxide (0·5 c.c.) for 3 days at room temperature, followed by acidification with 2N-sulphuric acid and treatment with aqueous 2 : 4-dinitrophenylhydrazine sulphate, gave *trans*-2-decalone 2 : 4-dinitrophenylhydrazone (0·012 g., 95%), which after recrystallisation from ethyl acetate had m. p. and mixed m. p. 173—174°.

cis-*Hydroxylation of* trans-Δ[2]-*Octalin*.—Prepared by Leroux's method,[2] *trans*-Δ[2]-octalin had b. p. 188—190°, n_D^{22} 1·4832; it probably [3] contained *ca.* 10% of Δ[1]-octalin.

The olefin (6 g.), acetic acid (380 c.c.), water (1 c.c.), and silver acetate (16 g.) were stirred at room temperature during the gradual (30 min.) addition of iodine (11 g.) and for a further 3 hr. The mixture was heated on the steam-bath for another 3 hr., then cooled, filtered, and concentrated under reduced pressure. The residue was treated with methanol (300 c.c.) and filtered again. The solution was brought to pH 10 with methanolic potassium hydroxide and then treated with a solution of potassium hydroxide (5 g.) in methanol (100 c.c.) for 18 hr. at room temperature under nitrogen. Neutralisation with 50% aqueous acetic acid followed by removal of the alcohol under reduced pressure gave an oily suspension which solidified. This was washed with a little water and dissolved in methanol. The solution was decolorised with charcoal, concentrated to small volume, and diluted with a little water, to give *trans*-decalin-2α : 3α-diol (3·2 g., 42·7%), flakes, m. p. and mixed m. p. 141°.

The mother liquor was diluted with more water, and set aside. After several days the solid which had separated was collected, dissolved in hot water and treated with charcoal. From the colourless solution, trans-*decalin*-cis-1 : 2-*diol* (0·15 g., 2%), crystallised in long needles, m. p. 109° (Found: C, 70·3; H, 10·5. $C_{10}H_{18}O_2$ requires C, 70·5; H, 10·65%). A few minutes' oxidation of this diol (0·03 g.) with potassium permanganate (0·035 g.) in water (3 c.c.) on the steam-bath followed by filtration gave a solution which was washed several times with ether and then acidified with dilute sulphuric acid. Extraction with ether followed by removal of the solvent and crystallisation of the solid from water gave β-*trans*-2-carboxy*cyclo*hexylpropionic acid, m. p. 138—139°. A mixed m. p. was the same as that of an authentic specimen, 142°. The 1 : 2-diol was derived from the small proportion of *trans*-Δ[1]-octalin present in the original olefin. By analogy with the stereochemical mode of *cis*-addition to steroid olefins by this method,[19] the product was probably the 1β : 2β-diol.

Epimerisation of trans-*Decalin*-2α : 3α-*diol*.—To the solution obtained by reaction of sodium

[19] Klass, Fieser, and Fieser, *J. Amer. Chem. Soc.*, 1955, **77**, 3829; Henbest, *J.*, 1957, 926; Shoppee, Jones, and Summers, *ibid.*, p. 3100.

XUM

(0·5 g.) with ethanol (20 c.c.) the diol (0·4 g.) was added. The mixture was heated at 170° for 5 hr., then cooled, neutralised with hydrochloric acid, and evaporated to dryness. The residue was extracted four times with boiling light petroleum (b. p. 80—100°), and the extracts were evaporated to a solid which was freed from a small amount of oily impurity by drainage on porous tile. Recrystallisation from benzene then afforded *trans*-decalin-2α : 3β-diol, m. p. and mixed m. p. 168°; a further crop was obtained by concentration of the mother liquor (total yield, 0·26 g.).

trans-*Decalin*-2α : 3α-*diol* 2-*Monotoluene*-p-*sulphonate*.—Toluene-*p*-sulphonyl chloride (2·23 g.) in pure chloroform (30 c.c.) was added in small portions to the 2α : 3α-diol (2 g.) in pyridine (10 c.c.) during 4 days at 0°. The mixture was kept at 0° for a further 24 hr. and was then diluted with chloroform and washed with water, dilute sulphuric acid, aqueous sodium hydrogen carbonate, and again with water. Removal of the solvent from the dried (Na_2SO_4) solution and two recrystallisations from aqueous methanol gave trans-*decalin*-2α : 3α-*diol* 2-*monotoluene*-p-*sulphonate* (3 g., 78%), m. p. 113° (Found: C, 62·8; H, 7·55; S, 9·7. $C_{17}H_{24}O_4S$ requires C, 62·95; H, 7·5; S, 9·9%).

Treatment of this derivative (0·03 g.) with 2N-methanolic sodium methoxide (1 c.c.) for 18 hr. at room temperature, followed by acidification with sulphuric acid and addition of 2 : 4-dinitrophenylhydrazine sulphate solution, gave *trans*-2-decalone 2 : 4-dinitrophenylhydrazone (0·02 g., 80%), which after recrystallisation from ethyl acetate had m. p. and mixed m. p. 174°.

trans-*Decalin*-2α : 3α-*diol Ditoluene*-p-*sulphonate*.—(i) A solution of the 2α : 3α-diol (0·1 g.) and toluene-*p*-sulphonyl chloride (0·3 g.) in dry pyridine (1 c.c.) was kept for 48 hr. at room temperature and then treated with crushed ice; the precipitate was crystallised from methanol, giving the 2α : 3α-*ditoluene*-p-*sulphonate* (0·04 g., 14%), prisms, m. p. 151° (Found: C, 60·3; H, 6·4; S, 13·2. $C_{24}H_{30}O_6S_2$ requires C, 60·2; H, 6·3; S, 13·4%). The mother liquor, on dilution with water, gave a solid which after several recrystallisation from aqueous methanol gave the 2-monotoluene-*p*-sulphonate (0·15 g., 78%), m. p. and mixed m. p. 112°.

(ii) Treatment of the 2-monotoluene-*p*-sulphonate (0·20 g.) with toluene-*p*-sulphonyl chloride (0·14 g.) in pyridine for 96 hr. at room temperature, followed by dilution with water, gave a solid, m. p. 118—125°, which after recrystallisations from methanol gave the 2α : 3α-ditoluene-*p*-sulphonate (0·15 g., 50%), m. p. and mixed m. p. 151°.

trans-*Decalin*-2α : 3α-*diol* 3-*Acetate* 2-*Toluene*-p-*sulphonate*.—A mixture of acetic anhydride (1·4 g.), pyridine (9 c.c.), and *trans*-decalin-2α : 3α-diol 2-monotoluene-*p*-sulphonate (1·4 g.) was kept for 5 days at room temperature. Dilution with water gave a solid which on recrystallisation from aqueous methanol formed the 2α : 3α-*diol* 3-*acetate* 2-*toluene*-p-*sulphonate* (1·53 g., 97%), needles, m. p. 122° (Found: C, 62·6; H, 7·4; S, 8·4. $C_{19}H_{26}O_5S$ requires C, 62·3; H, 7·15; S, 8·75%). Treatment of this derivative with 2N-methanolic sodium methoxide, as described above for the monotoluene-*p*-sulphonate, gave *trans*-decalin-2-one, isolated as the 2 : 4-dinitrophenylhydrazone (90%), m. p. and mixed m. p. 173—174°.

trans-*Decalin*-2β : 3α-*diol Diacetate*.—A solution of *trans*-decalin-2α : 3α-diol 3-acetate 2-toluene-*p*-sulphonate (0·81 g.) and potassium acetate (0·62 g.) in acetic acid (10 c.c.) and acetic anhydride (5 c.c.) was heated for 12 hr. on the steam-bath and then boiled under reflux for 18 hr. Dilution of the cooled mixture with water, followed by neutralisation with solid sodium hydrogen carbonate and extraction with ether, gave a crude product, m. p. 107—112°; the m. p. of a mixture with the original compound was 115—117°.

The recovered material was then boiled under reflux with sodium acetate (2 g.) in acetic anhydride (15 c.c.) for 48 hr. The mixture was then cooled and worked up as above to give a liquid, which on distillation gave an oil (0·1 g.), b. p. 78—120°/3 mm., n_D^{20} 1·4769. Recrystallisation of the solidified oil from aqueous methanol gave *trans*-decalin-2β : 3α-diol diacetate, flakes, m. p. 85° (the reported [2,3] m. p. for the diacetate of a *trans*-decalin-*trans*-2 : 3-diol is 85°).

Treatment of this diacetate under reflux with a trace of sodium methoxide in methanol (5 c.c.) for 30 min. followed by evaporation to dryness, trituration with a few drops of water, and crystallisation from aqueous methanol gave *trans*-decalin-2β : 3α-diol, m. p. and mixed m. p. 163°.

Reduction of 3-*Oxo*-cis-*decalin*-2α-*ol*.—A solution of the ketol [1] (0·25 g.) in dry ether (15 c.c.) was added to a stirred solution of lithium aluminium hydride (0·6 g.) in dry ether (20 c.c.). The mixture was then refluxed for an hour and worked up as described for the reduction of the *trans*-ketol giving a solid (0·23 g., 90%), m. p. 75—85°, which was dissolved in acetone (40 c.c.) containing sulphuric acid (0·1 c.c.). After 24 hr. at room temperature, the solution was

XUM

neutralised with concentrated ammonia, filtered, and evaporated to an oil, which was diluted with light petroleum (b. p. 80—100°) (2 c.c.). The precipitate was crystallised from ether to give cis-*decalin*-2α : 3β-*diol* (0·02 g., 10%), long needles, m. p. 125° (Found: C, 70·4; H, 10·7. $C_{10}H_{18}O_2$ requires C, 70·5; H, 10·65%). Infrared absorption: see Table. Reaction of the diol with a slight excess of toluene-*p*-sulphonyl chloride in pyridine for 3 days at room temperature gave the *ditoluene*-p-*sulphonate*, prisms (from methanol), m. p. 126—127° (Found: C, 60·5; H, 6·5; S, 13·3. $C_{24}H_{30}O_6S_2$ requires C, 60·2; H, 6·3; S, 13·4%).

The petroleum solution remaining after isolation of the above diol was evaporated and the residue distilled to give 2α : 3α-iso*propylidenedioxy*-cis-*decalin* (0·07 g., 27%), b. p. 118°/10 mm. (Found: C, 74·1; H, 10·6. $C_{13}H_{22}O_2$ requires C, 74·2; H, 10·5%). This derivative (0·06 g.) was heated on the steam bath for 1 hr. with 2N-sulphuric acid (4 c.c.), and the cooled solution then extracted with ether to give a solid, recrystallisation of which from light petroleum (b. p. 60—80°) gave cis-*decalin*-2α : 3α-*diol* (0·03 g.), m. p. 100° (Found: C, 70·4; H, 10·7. $C_{10}H_{18}O_2$ requires C, 70·5; H, 10·65%); infrared absorption: see Table.

Reduction of 3-*Oxo*-cis-*decalin*-2β-*yl Acetate*.—The 2β-acetate [1] (0·42 g.) was reduced with lithium aluminium hydride (0·6 g.) in boiling ether (35 c.c.) as described above. The product (0·28 g., 82%), m. p. 114—116°, was treated with acetone containing a trace of sulphuric acid and worked up in the same way to give *cis*-decalin-2α : 3β-diol (0·15 g., 53%), m. p. and mixed m. p. 125°, and 2β : 3β-iso*propylidenedioxy*-cis-*decalin* (0·08 g., 23%), b. p. 119°/11 mm. (Found: C, 74·1; H, 10·8. $C_{13}H_{22}O_2$ requires C, 74·2; H, 10·5%). Hydrolysis of the *iso*propylidene compound (0·07 g.) with 2N-sulphuric acid gave cis-*decalin*-2β : 3β-*diol* (0·03 g.), needles (from light petroleum, b. p. 80—100°), m. p. 118° (Found: C, 70·8; H, 10·95. $C_{10}H_{18}O_2$ requires C, 70·5; H, 10·65%); infrared absorption: see Table.

Hydrogenation of trans-2 : 3-*Diacetoxytetralin*.—*trans*-2 : 3-Diacetoxytetralin (0·9 g.) [obtained from the hydrogenation products of naphthalene-2 : 3-diol (see below)], dissolved in acetic acid (20 c.c.) containing a few drops of ethanolic hydrogen chloride,[20] was hydrogenated over platinum oxide (0·05 g.) at 17° and 764 mm.; 253 c.c. of hydrogen were absorbed during 24 hr. (calc.: 257 c.c.). The filtered solution was evaporated and the residue was dissolved in ether, washed with aqueous sodium hydrogen carbonate, and with water, and dried ($MgSO_4$). Removal of the solvent followed by distillation of the residue afforded cis-*decalin*-2α : 3β-*diol diacetate* (0·6 g., 65%), b. p. 110°/2 × 10^{-3} mm., n_D^{23} 1·4756 (Found: C, 66·2; H, 8·8; O, 25·1. $C_{14}H_{22}O_4$ requires C, 66·1; H, 8·7; O, 25·2%).

Treatment of the diacetate with a trace of sodium methoxide in dry methanol under reflux for 30 min., and recrystallisation of the product from ether, gave *cis*-decalin-2α : 3β-diol, m. p. and mixed m. p. 125°.

cis-2 : 3-*Diacetoxytetralin*.—Treatment of *cis*-tetralin-2 : 3-diol monoacetate [18] (2·1 g.) with acetic anhydride (1·4 g.) in pyridine (8 c.c.) for 48 hr. at room temperature, followed by dilution with water and crystallisation from aqueous methanol, gave *cis*-2 : 3-diacetoxytetralin (2·2 g., 87%), prisms, m. p. 58° (lit.,[3] m. p. 59°).

Hydrogenation of cis-2 : 3-*Diacetoxytetralin*.—The diacetate (2·16 g.) in acetic acid (25 c.c.) was hydrogenated over platinum oxide (0·1 g.) at 19° and 768 mm. for 96 hr.; 595 c.c. of hydrogen were absorbed. Working up of the product as described for the *trans*-isomer gave a diacetate (1·93 g., 87%), b. p. 102°/3 × 10^{-3} mm., n_D^{23} 1·4722—1·4805 (Found: C, 66·3; H, 8·7. Calc. for $C_{14}H_{22}O_4$: C, 66·1; H, 8·7%). Catalytic deacetylation of this product with methanolic sodium methoxide gave a solid, m. p. 78—84°, which was fractionally crystallised from light petroleum (b. p. 80—100°), giving *cis*-decalin-2α : 3α-diol (0·3 g.), m. p. and mixed m. p. 100°, as the less soluble fraction. The more soluble component could not be isolated pure.

Hydrogenation of Naphthalene-2 : 3-*diol*.—The technical grade material was treated in boiling benzene first with charcoal and then with Raney nickel. Recrystallisation from benzene then gave a colourless product, m. p. 162° [lit.,[21] m. p. 163·5—164° (corr.)]. This (50 g.) was hydrogenated in ethanol (200 c.c.), containing platinum oxide (0·4 g.), at 125° and 100 atm. until absorption ceased (78 hr.). The mixture was filtered and evaporated; the semi-solid residue was mixed with 10% aqueous sodium hydroxide (250 c.c.) and extracted with ether. Solvent was removed from the dried (Na_2SO_4) extract, and the residue (11·6 g.) fractionally crystallised from benzene, giving, as the less soluble fraction (7·6 g.), the molecular compound, m. p. 141°, of tetralin-2 : 3-*cis*- and -*trans*-diol (Found: C, 72·9; H, 7·5. Calc. for $C_{10}H_{12}O_2$:

[20] Brown, Durand, and Marvel, *J. Amer. Chem. Soc.*, 1936, **58**, 1594.
[21] Machek and Sitzber, *Monatsh.*, 1933, **62**, 195.

C, 73·1; H, 7·4%) [lit.,[22] m. p. 141·8—142·8° (corr.)]. The more soluble fraction gave tetralin-*cis*-2 : 3-diol, m. p. 120—121° (Found: C, 73·4; H, 7·5%) (lit.,[22] m. p. 124—125°).

The aqueous layer was acidified with dilute sulphuric acid and extracted with ether. Removal of the solvent from the dried (Na_2SO_4) extract and crystallisation of the residue from benzene gave unchanged naphthalene-2 : 3-diol (13·8 g.), m. p. and mixed m. p. 160°.

The molecular compound, m. p. 141° (7 g.), was treated with acetic anhydride (9·5 g.) in pyridine (10 g.) and benzene (200 c.c.) according to Leroux's method.[2] The oily product (9·9 g.) was dissolved in ethanol and cooled in ice whereupon *trans*-2 : 3-diacetoxytetralin (2·6 g.), m. p. 110°, separated (Found: C, 67·9; H, 6·3. Calc. for $C_{14}H_{16}O_4$: C, 67·7; H, 6·5%) (lit.,[2] m. p. 111°). Deacetylation of a portion of this diacetate gave tetralin-*trans*-2 : 3-diol, m. p. and mixed m. p. 135—136°.

Rates of Oxidation with Lead Tetra-acetate.—Cordner and Pausacker's method [23] was used, solutions (*ca.* 0·02M) of the diols in acetic acid being mixed with equal volumes of a 0·0365M-solution of lead tetra-acetate in acetic acid at 25°. Plots of $\log b(a - x)/a(b - x)$ against t were linear, and the bimolecular rate constants were calculated from the expression $k = (2{\cdot}303 \times \text{slope})/(a - b)$. Results are shown in the Table.

Rates of Oxidation with Sodium Metaperiodate.—(i) *trans*-Decalin-2β : 3α-diol (55·0 mg.) was dissolved in ethanol (2 c.c.) and diluted with water to 25 c.c. A 5-c.c. portion was mixed at 20° with 5 c.c. of 0·0224M-aqueous sodium metaperiodate, and after a known time the reaction was stopped by the addition of 5 c.c. of 10% potassium iodide in N-sulphuric acid and the liberated iodine titrated with thiosulphate. A blank experiment was carried out under the same conditions with no diol. The % reaction was: 24 (2·5 min.), 50 (7 min.), 62 (10·5 min.), 98 (120 min.), and the bimolecular rate constant for the first three determinations 10·4, 10·6, and 10·7 $mole^{-1}$ l. $min.^{-1}$.

(ii) A solution of *trans*-decalin-2α : 3β-diol (60·1 mg.) was prepared and used in exactly the same way. The % reaction was: 66 (1 min.), 73 (1·5 min.), 85 (2·5 min.), 100 (15 min.), and k_2 for the first three determinations 131, 113, and 114 $mole^{-1}$ l. $min.^{-1}$. Owing to the very rapid reaction, these figures can only be regarded as approximate.

We thank Dr. M. U. S. Sultanbawa, University of Ceylon, for a generous gift of *trans*-decalin-2α-ol.

Department of Organic Chemistry, Imperial College of Science and Technology, South Kensington, London, S.W.7. [*Received, December 5th*, 1957.]

[22] Verkade, Coops, Maan, and Verkade-Sandbergen, *Annalen*, 1928, **467**, 217.
[23] Cordner and Pausacker, *J.*, 1953, 102.

---

436. *Stages in Oxidations of Organic Compounds by Potassium Permanganate. Part IX.* Oxidation of Allyl Alcohol by Manganic Pyrophosphate.*

By Haring Land and William A. Waters.

Allyl and crotyl alcohol are very slowly oxidised by manganic pyrophosphate. The reaction order with respect to Mn^{III} is complex, becoming of first order at high Mn^{III} concentrations. Manganous ions retard the oxidation but this retardation reaches a limiting value. Peroxidic impurities have a noticeable immediate effect. Suggestions concerning the reaction mechanism are advanced.

Although acid manganic pyrophosphate does not oxidise either monohydric alcohols or olefins [1] it slowly attacks allyl alcohol and we have studied this reaction kinetically. The slow oxidation cannot be followed titrimetrically by adding portions to aqueous potassium iodide since the combination of iodine with allyl alcohol has a significant velocity at room temperature. However, though manganic pyrophosphate does not react directly with

* Part VIII, *J.*, 1957, 4312.

[1] Drummond and Waters, *J.*, 1953, 440.

XUM

arsenite a trace of iodide causes immediate reduction of Mn^{III} and, in a bicarbonate buffer, arsenite can be titrated with iodine under conditions in which there is negligible addition of iodine to allyl alcohol provided that air-free conditions are maintained and the arsenite solutions are neutralised immediately the reduction of Mn^{III} is visibly complete.

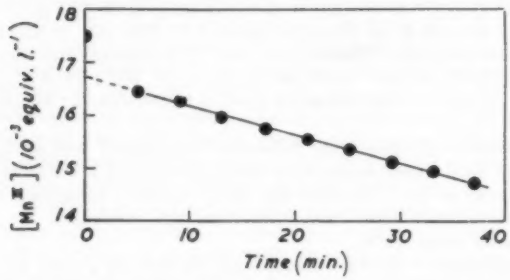


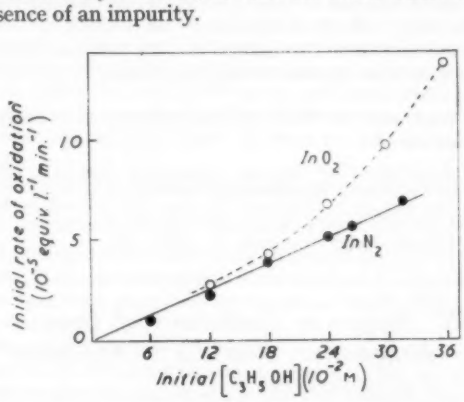
FIG. 1. *Typical initial stage of an oxidation of allyl alcohol by manganic pyrophosphate.*

Initial concns.: $[Mn^{III}]$ $1{\cdot}75 \times 10^{-2}$M; $[C_3H_5{\cdot}OH]$ 0·20M; [pyrophosphate] 0·086M; pH 0·1.

At 45°, with allyl alcohol in large excess, excellent initial rate constants could be obtained though a slight immediate drop of titre was always noted (see Fig. 1). When this small drop is neglected the initial rate measurements show that the consumption of Mn^{III} is a first-order process with respect to allyl alcohol in absence of oxygen (Table 1) but becomes of higher order in its presence (Fig. 2). The rate constants themselves were independent of the source or method of purification of the allyl alcohol, so that the main oxidation, though slow, does not depend on the presence of an impurity.

FIG. 2. *Dependence of initial rate on allyl alcohol concentration.*

Initial concns.: $[Mn^{III}]$ $1{\cdot}75 \times 10^{-2}$M; [pyrophosphate] 0·086M; pH 0·10.



The order with respect to $[Mn^{III}]$ is complex and appears to be the sum of a first-order process and one that approaches a limiting value (Fig. 3). Manganous ions specifically affect this rate; at low $[Mn^{II}]/[Mn^{III}]$ ratios the oxidation is retarded by them but a lower

TABLE 1. *Oxidation of allyl alcohol under nitrogen at* 45°.

Initial $[Mn^{III}]$ $1{\cdot}75 \times 10^{-2}$N. Total pyrophosphate 0·086M. pH 0·2.

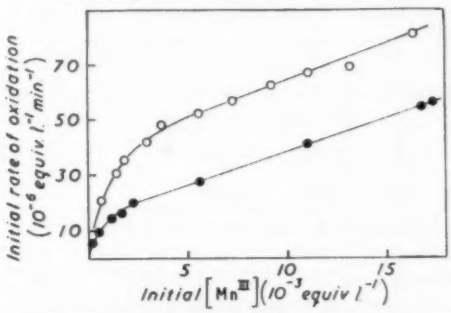
Initial $[C_3H_5{\cdot}OH]$ (10^{-2}M)	20·0	16·7	13·3	11·1	8·3	5·6	2·8
Initial $-d[Mn^{III}]/dt$ (10^{-6} mole l.$^{-1}$ min.$^{-1}$)	5·7	4·9	3·8	3·2	2·6	1·6	1·0
Initial rate/$[C_3H_5{\cdot}OH]$	2·85	2·93	2·85	2·88	3·13	2·86	2·8

limit, at which the reaction velocity is about halved, is soon reached, and at high $[Mn^{II}]/[Mn^{III}]$ ratios the rate of oxidation shows a slight upward trend (Fig. 4). Since high concentrations of zinc ions produce a corresponding effect the gradual increase in rate may possibly be due to the formation of sufficient manganous or zinc pyrophosphate to diminish significantly the concentration of free pyrophosphate anions in the solution. This change

would increase the oxidation potential of the reagent for, as in other cases of oxidation by manganic pyrophosphate, the rate of oxidation of allyl alcohol is decreased by increasing the pyrophosphate concentration and increased by increasing the acidity. A more cursory examination of the oxidation of crotyl alcohol showed that it was somewhat faster but had similar kinetic features.

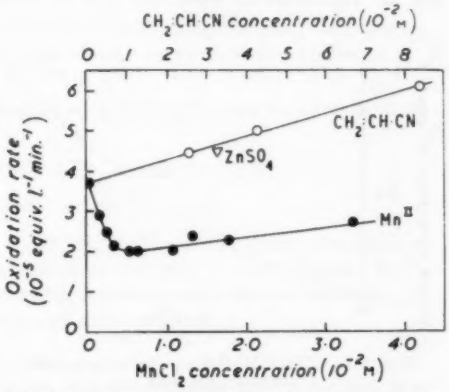
The oxidation of allyl alcohol by manganic pyrophosphate must generate free radicals, for the oxidising mixture can absorb oxygen and catalyse the polymerisation of vinyl cyanide (which is not attacked by manganic pyrophosphate alone [2]). Addition of this monomer to the oxidising allyl alcohol increases the consumption of Mn^{III} (Fig. 4, top line). A more marked effect of the same character had been found in the oxidation of malonic

FIG. 3. *Dependence of initial rate on* $[Mn^{III}]$.



Initial concns.: [pyrophosphate] 0·086M; Upper curve: $[C_3H_5{\cdot}OH]$, 0·30M; pH 0·35; Lower curve: $[C_3H_5{\cdot}OH]$ 0·20M; pH 0·20.

FIG. 4. *Dependence of initial rate on* $[Mn^{II}]$ *and on* $[CH_2{:}CH{\cdot}CN]$.



Initial concns.: $[Mn^{III}]$ $1{\cdot}53 \times 10^{-3}$M; [pyrophosphate] 0·078M; $[C_3H_5{\cdot}OH]$ 0·133M; pH 0·20.

acid.[3] Again the oxidising system can induce the reduction of mercuric chloride,[2] but it does not promote the oxidation of propan-2-ol.[3]

The Reaction Mechanism.—For the straight portion of the graphs of Fig. 3 the limiting rate equation becomes:

$$-d[Mn^{III}]/dt = \text{Const. } [Mn^{III}] \,.\, [C_3H_5{\cdot}OH] \,.\, [H^+]$$

The dependence of the rate on acidity may well be due to the effect of acidity on the redox potential of complexed manganic pyrophosphate [4] and it has not been studied in detail. The strict first-order dependence on $[C_3H_5{\cdot}OH]$ shows that the formation of a ternary (manganic–allyl alcohol–pyrophosphate) complex is not a prerequisite of the oxidation as it is for a 1 : 2-glycol [5] or an α-hydroxy-acid.[6] Again spectrographic examination of reacting mixtures over the wave-band 200—500 μ gave no indication of the formation of transient manganic complexes. The initial reaction can therefore be visualised as a one-electron abstraction from the allyl alcohol (possibly coupled with proton loss), but the effects of both manganous and manganic ions at low concentrations show that reactions subsequent to the formation of the primary organic free radical can, in certain circumstances, be kinetically significant.

[2] Drummond and Waters, *J.*, 1953, 2836.
[3] *Idem*, *J.*, 1954, 2456.
[4] Kolthoff and Watters, *J. Amer. Chem. Soc.*, 1948, **70**, 2455.
[5] Drummond and Waters, *J.*, 1953, 3119.
[6] Levesley and Waters, *J.*, 1955, 217.

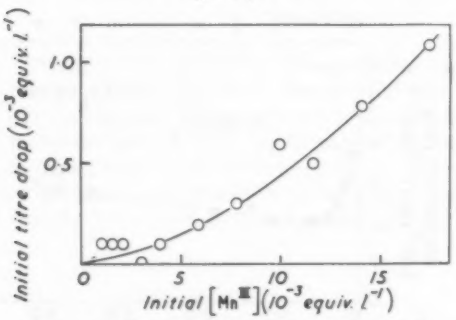
In Part IV [3] retardation of the oxidation of malonic acid by manganous ions was ascribed to the formation of an oxidising radical, *i.e.*:

$$\text{Substrate} + Mn^{III} \rightleftharpoons \text{Radical} + Mn^{II} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$\text{Radical} + Mn^{III} \longrightarrow \text{Product} + Mn^{II} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

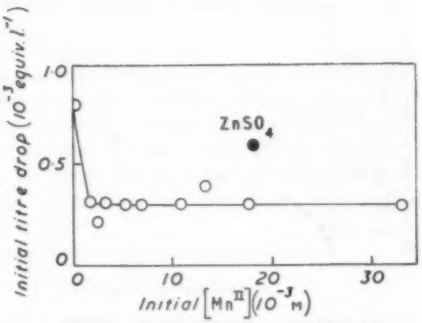
but equations of this type do not indicate how the retarding effect of manganous ions could reach a limiting value (cf. Fig. 4). One possibility that cannot altogether be excluded is that the reversible reaction (1) involves a molecular oxidation product of allyl alcohol, but it is difficult to reconcile such a reaction sequence with the rate-dependence on $[Mn^{III}]$ at low concentrations. It is more probable that the initial radical is removed by oxidation and reduction, as in equations (1) and (2), and partly by the bimolecular processes of

FIG. 5. *Dependence of initial titre drop on initial* $[Mn^{III}]$.



Concns.: $[C_3H_5{\cdot}OH]$ 0·30M; [pyrophosphate] 0·086M; pH 0·35.

FIG. 6. *Dependence of initial titre drop on initial* $[Mn^{II}]$.



Concns.: $[C_3H_5{\cdot}OH]$ 0·133M; $[Mn^{III}]$ $1{\cdot}53 \times 10^{-2}$M; [pyrophosphate] 0·078M; pH 0·20.

dimerisation or disproportionation that give inert products for, as Part VI [7] exemplifies, such reactions may be very fast. According to the scheme:

$$C_3H_5{\cdot}OH + Mn^{III} \rightleftharpoons R{\cdot} + Mn^{II} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

$$R{\cdot} + Mn^{III} \longrightarrow \text{Product I} + Mn^{II} \quad . \quad . \quad . \quad . \quad . \quad (4)$$

$$2R{\cdot} \longrightarrow \text{Products II} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

the reversibility of reaction (3) would cause manganous ions to depress the initial reaction velocity and at high Mn^{III} concentrations a sufficient radical concentration would build up to allow reaction (5) to predominate over (4), the forward reaction (3) then becoming rate-determining. However, though equations (3)—(5) accord with the observed rate-dependence on $[Mn^{III}]$ they do not indicate strict first-order dependence on $[C_3H_5{\cdot}OH]$ at low Mn^{III} concentrations. Though Table 1 does not indicate any departure from first-order reactivity it relates to the linear portion of the curves of Fig. 3; the oxidation was far too slow to be tested at low concentrations of both allyl alcohol and manganic pyrophosphate.

The acceleration of the oxidation by vinyl cyanide corresponds to a fast reaction (6), giving a radical that is more easily oxidised than the primary radical R·:

$$R{\cdot} + CH_2{:}CH{\cdot}CN \longrightarrow R{\cdot}CH_2{\cdot}CH(CN){\cdot} \quad . \quad . \quad . \quad . \quad . \quad (6)$$

This again was inferred in the investigation of the oxidation of malonic acid.[3]

Product investigation has not been practicable for the overall extent of the oxidation

[7] Drummond and Waters, *J.*, 1955, 497.

is slight and, as Part VIII [8] has shown, all the simple oxidation products of allyl alcohol are easily attacked by manganic pyrophosphate. Traces of formaldehyde and of formic acid which do resist the oxidative degradation have in fact been detected. Without definite evidence of the nature of the first oxidation product it is not possible to decide whether attack on allyl alcohol occurs initially at the CH_2·OH group or at the double bond.

The initial titre drop. This effect (see Fig. 1) was most evident in stored samples of allyl alcohol that gave a slight positive peroxide reaction (ferrous thiocyanate test), and was very greatly reduced, though not completely eliminated, by repeated fractionation of the allyl alcohol in purified nitrogen through a column packed with glass helices; metal gauze packings had an adverse effect. With any one batch of allyl alcohol the titre drop were proportional to the allyl alcohol concentration (Table 2); it increased with increasing concentration of Mn^{III} (Fig. 5), but manganous ions in quite low concentration specifically depressed it to a small but limited extent (Fig. 6). These effects are consistent with the

TABLE 2. *Initial drop in titre on oxidation of allyl alcohol with manganic pyrophosphate.*

$[C_3H_5$·OH] (10^{-2}M)	0·0	2·8	5·6	8·3	11·1	13·3	16·7	20
Initial $[Mn^{III}]$ extrapolated (10^{-2}M)	1·75	1·75	1·74	1·72	1·71	1·69	1·69	1·68

presence in the allyl alcohol of a very small amount of a hydroperoxide capable both of reducing Mn^{III} and of oxidising Mn^{II}, *i.e.*:

$$RO_2H + 2Mn^{3+} + H_2O = ROH + O_2 + 2Mn^{2+} + 2H^+$$

$$RO_2H + 2Mn^{2+} + 2H^+ = ROH + 2Mn^{3+} + H_2O$$

Reactions of these types have frequently been described.[9] These equations also explain why oxygen, which would yield RO_2· radicals, enhances the rate of reduction of Mn^{III} (Fig. 2). Indeed the initial titre drop may in part be due to a rapid removal by radicals, R·, of residual dissolved oxygen in the aqueous solution of the oxidant.

EXPERIMENTAL

Kinetic experiments were carried out with stirring in a three-necked flask immersed in a thermostat at 45° ± 0·3°. Purified nitrogen was continually passed through the reacting solutions and aliquot parts were removed by suction at a rate much less than that of the nitrogen flow. About 1 g. of sodium hydrogen carbonate was placed in each of a series of 250 ml. stoppered bottles together with enough dilute sulphuric acid to bring about the displacement of all air. To each bottle was added slightly more standard arsenite solution than that expected for complete reduction of the Mn^{III}, then 0·1 ml. of a 0·5% solution of potassium iodide, and finally the aliquot part of the reaction mixture. Immediately decolorisation was complete excess of sodium hydrogen carbonate was added and the remaining arsenite was titrated with standard iodine with starch as indicator.

Allyl alcohol, dried by azeotropic distillation with benzene, was repeatedly distilled in purified nitrogen through a column filled with Fenske helices, the fraction of b. p. 96·5° being collected and stored in the dark under nitrogen. When required, weighed sample were dissolved in boiled-out distilled water. To avoid contamination, smallish samples were stored in sealed ampoules, unused material from opened ampoules being returned for refractionation.

Neither commercial samples of allyl alcohol, nor material prepared in the laboratory from glycerol, could be freed completely from peroxides. However, all samples after purification as described above were oxidised at the same rate after the first few minutes.

Material fractionated through a column packed with nickel gauze had a high peroxide content and tended to polymerise.

Manganic pyrophosphate solutions were prepared by the method described in earlier parts of this series.

Results are recorded in Tables 1 and 2 and Figs. 1—6.

One of us (H. L.) thanks the British Council for a Scholarship.

THE DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, December 12th*, 1957.]

[8] Land and Waters, *J.*, 1957, 4312.
[9] Kharasch, Fono, Nudenberg, and Bischoff, *J. Org. Chem.*, 1952, **17**, 207.

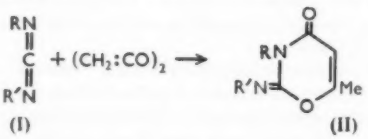
437. *Derivatives of Acetoacetic Acid. Part IX.* The Reaction of Diketen with Carbodi-imides.*

By R. N. Lacey and W. R. Ward.

Diketen reacts with carbodi-imides to give 2 : 3-dihydro-2-imino-4-oxo-1 : 3-oxazine derivatives such as have previously been prepared from diketen and *NN'*-disubstituted derivatives of *S*-alkylthiourea. Certain unsymmetrical carbodi-imides gave single products for which structural evidence was afforded by hydrolysis. Infrared and ultraviolet spectroscopic evidence in this field is reported.

Condensation products of keten, substituted ketens, and keten dimers with carbodi-imides have been described in a recent German patent [1] assigned to Farbenfabriken Bayer Aktiengesellschaft of Leverkusen. As typical carbodi-imides falling within the scope of their claims, the Bayer workers listed, amongst others, *NN'*-di*iso*propyl-, *N-tert.*-butyl-*N'-cyclo*hexyl-, *NN'*-di*cyclo*hexyl-, and *N-cyclo*hexyl-*N'-tert.*-octyl-carbodi-imide, and examples of the reaction of these derivatives with diketen were given. Arylcarbodi-imides, *e.g.*, *N-tert.*-butyl-*N'*-phenylcarbodi-imide and *NN'*-diphenylcarbodi-imide were also quoted as possible starting materials but no experimental details of examples involving arylcarbodi-imides were given. In all the examples involving reaction of diketen with carbodi-imides, good yields of sharp-melting solid products were obtained. No analyses for these solid products were given and no suggestions as to their structure were made; they were described as hitherto unknown addition compounds.

We found the reaction of diketen with *NN'*-dialkylcarbodi-imides to proceed smoothly in boiling benzene, to give good yields of crystalline products in agreement with the findings of the German workers. Analytical values were consistent with the supposition that the products arose from the simple addition of one mole of diketen to one mole of the carbodi-imide. The reaction of *NN'*-diethylcarbodi-imide with diketen, not described in the above patent, gave direct structural evidence for this group of compounds since the product so obtained proved to be identical with that previously obtained [2] by one of us from the reaction of diketen with *NN'*-diethyl-*S*-methyl*iso*thiourea with the elimination of methanethiol. The reaction of carbodi-imides with diketen may therefore be formulated as below, the products being 2-imino-1 : 3-oxazine derivatives of general formula (II).



(I) (II)

Comparison of the infrared spectrum of the product arising from *NN'*-diethylcarbodi-imide with that of authentic (II; R = R' = Et) afforded structural confirmation, and infrared spectroscopic evidence (see Table 4) showed that the products arising from [I; R = R' = Pr^i; R = R' = *cyclo*hexyl; R = *cyclo*hexyl, R' = Bu^t; and R = *cyclo*hexyl, R' = 1 : 1 : 3 : 3-tetramethylbutyl (" *tert.*-octyl ")] had the same general structure. The ultraviolet spectroscopic evidence, presented in Table 1, was in general agreement.

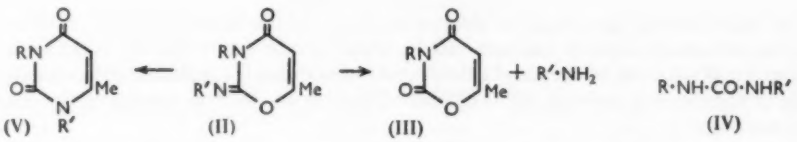
The oxazines (II, where R and R' are both alkyl) are weak bases and dissolve in dilute hydrochloric acid. Potentiometric titration with perchloric acid in acetic acid showed a sharp inflection denoting a monoacid base; pK values ($\pm$ 0·05) for certain of these

* Part VIII, *J.*, 1954, 854.

[1] Hofmann, Schmidt, Wamsler, Reichle, and Moosmüller, G.P. 960,458 (21/3/57).
[2] Lacey, *J.*, 1954, 845.

derivatives were: R = R′ = Et 9·35, R = R′ = Pr^{i} 9·85, R = *cyclo*hexyl, R′ = Bu^{t} 10·70.

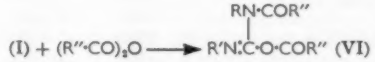
Acid-hydrolysis of the oxazines (II; R = R′ = *cyclo*hexyl; R = R′ = Pr^{i}) afforded not only the corresponding dioxo-oxazines (III) with a mole of aliphatic amine as found previously [2] for (II; R = R′ = Et), but also the ureas (IV) and the isomeric uracils (V). Formation of the last two types of product had previously been observed with only the aromatic substituted oxazines (II).



Hydrolysis of the compound (II; R = *cyclo*hexyl, R′ = Bu^{t}) with dilute hydrochloric acid (3%) gave the dione (III; R = *cyclo*hexyl) and, the urea (IV; R = *cyclo*hexyl, R′ = Bu^{t}) and some *cyclo*hexylurea. The use of stronger acid (15%) gave the dioxo-oxazine and *cyclo*hexylurea but none of the dialkylurea. It was established that the urea (IV; R = *cyclo*hexyl, R′ = Bu^{t}) is converted into *cyclo*hexylurea in high yield with removal of the elements of *iso*butene by heating in the presence of acid. This reaction is effectively the reverse of that disclosed by Harvey and Caplan,[3] who showed that urea can be converted into a *tert.*-alkylurea by treatment with a tertiary alcohol in the presence of sulphuric acid. Hydrolysis of the oxazine (II; R = *cyclo*hexyl, R′ = 1 : 1 : 3 : 3-tetramethylbutyl) with hydrochloric 15% acid similarly gave the dione (III; R = *cyclo*hexyl) and *cyclo*hexylurea; the urea (IV; R = *cyclo*hexyl, R′ = 1 : 1 : 3 : 3-tetramethylbutyl) afforded *cyclo*hexylurea in almost quantitative yield on treatment with boiling 15% hydrochloric acid.

The reaction of arylcarbodi-imides with diketen in boiling benzene was found to be slow but, in agreement with the claim of Hofmann *et al.*,[1] the condensation was catalysed by cuprous chloride. *NN′*-Diphenylcarbodi-imide gave the known [2] oxazine (II; R = R′ = Ph) and *N-cyclo*hexyl-*N′*-phenylcarbodi-imide gave (II; R = *cyclo*hexyl, R′ = Ph), both preparations giving low yields. The structure of the latter oxazine was established by hydrolysis to the dione (III; R = *cyclo*hexyl) and *N-cyclo*hexyl-*N′*-phenylurea. The reaction of diketen with *N*-benzyl-*N′*-phenylcarbodi-imide was catalysed by toluene-*p*-sulphonic acid, giving a small yield of the uracil (V; R = Ph·CH$_2$, R′ = Ph) formed, very possibly, by the known [2] acid-catalysed re-arrangement of the imino-oxazine (II; R = Ph·CH$_2$, R′ = Ph).

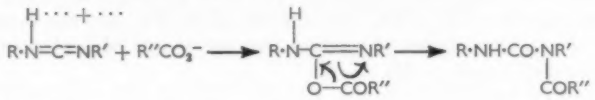
Diketen may be formally regarded as the inner anhydride of acetoacetic acid. Schulz and Fiedler [4] have suggested that acid anhydrides react with carbodi-imides to give *ON*-diacylureas (VI) (they did not isolate reaction products of this type but, after the addition of water, obtained *N*-acylureas), products analogous to the oxazines (II) derived from diketen.



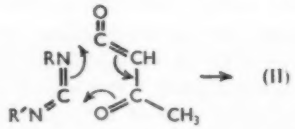
The orientation of the attack of the diketen molecule upon the unsymmetrical carbodi-imides deserves comment. Khorana [5] showed that in the reaction of carboxylic acids with *N-cyclo*hexyl-*N′*-phenylcarbodi-imide the acyl group was attached to the less basic nitrogen atom of the original carbodi-imide, *i.e.*, that adjacent to the phenyl group, and postulated that the reaction proceeded by a three-step mechanism in which the more

[3] Harvey and Caplan, U.S.P. 2,247,495 (15/4/38).
[4] Schulz and Fiedler, *Chem. Ber.*, 1956, **89**, 2681.
[5] Khorana, *J.*, 1952, 2083.

basic nitrogen atom is first attacked by a proton, this being followed by nucleophilic attack of the acid anion and re-arrangement as shown:



The orientation of the attack of diketen is clearly in the opposite sense. *N*-Alkyl-*N'*-phenylcarbodi-imides afford oxazines (II) in which attack has evidently occurred at the nitrogen atom adjacent to the alkyl substituent; this result is consistent with electrophilic attack of the diketen molecule on the point of maximum electron-density in the carbodi-imide molecule:



When R' is *tert.*-alkyl, the inductive effect of the substituent directs attack at the nitrogen atom remote from this substituent. It follows from the above that the attack of a carboxylic anhydride on an unsymmetrical carbodi-imide should take place at the

TABLE 1. *Oxazines* (II).

	$\lambda_{max.}$ (Å)	$\varepsilon_{max.}$
(II; R = R' = *cyclo*hexyl)	2620	1950
(II; R = R' = Pr^i)	2580	1950
(II; R = *cyclo*hexyl, R' = Bu^t)	2580	2000
(II; R = R' = Et)	2580	2050
(II; R = *cyclo*hexyl, R = C_8H_{17} [a])	2590	1800
(II; R = Me, R' = Ph)	2485	12,300
(II; R = *cyclo*hexyl, R' = Ph)	2500	11,700
(II; R = Ph·CH_2, R' = Ph)	2510	12,800
(II; R = R' = Ph)	*ca.* 2490	12,400

TABLE 2. *Oxazines* (III).

	$\lambda_{max.}$ (Å)	$\varepsilon_{max.}$
(III; R = Me)	2270	7500
(III; R = Et)	2270	7900
(III; R = Pr^i)	2270	7900
(III; R = *cyclo*hexyl)	2275	8200
(III; R = Ph·CH_2)	2275	9000
(III; R = Ph)	2310	10,400

TABLE 3. 6-*Methyluracils* (V).

	$\lambda_{max.}$ (Å)	$\varepsilon_{max.}$	$\lambda_{min.}$ (Å)	$\varepsilon_{min.}$
(V; R = Me, R' = H)	2590	9100	2320	2300
(V; R = Et, R' = H)	2610	9500	2320	2300
(V; R = Pr^i, R' = H)	2615	8600	2320	2300
(V; R = *cyclo*hexyl, R' = H)	2620	8300	2340	2600
(V; R = Ph·CH_2, R' = H)	2615	8800	2360	2800
(V; R = Ph, R' = H)	2620	9800	2320	3600
(V; R = R' = Me)	2660	10,600	2340	2100
(V; R = R' = Pr^i)	2685	10,900	2380	2400
(V; R = R' = *cyclo*hexyl)	2710	10,500	2380	2600
(V; R = Me, R' = Ph·CH_2)	2660	11,400	2350	2600
(V; R = Me, R' = Ph)	2635	11,200	2350	3700
(V; R = Ph·CH_2, R' = Me)	2680	9400	2380	2400
(V; R = Ph, R' = Me)	2680	10,600	2380	3400
(V; R = Ph·CH_2, R' = Ph)	2640	12,100	2380	4200

[a] C_8H_{17} = 1 : 1 : 3 : 3-tetramethylbutyl.

more basic nitrogen atom, *i.e.*, the opposite orientation to that observed with a carboxylic acid; this question merits further study.

The ultraviolet light absorption evidence shown in Tables 1 and 2 is in agreement with the formulations assigned. The strong absorption exhibited at about 2500 Å by the compounds (II) having R' = Ph is characteristic of the Ph·N:C system. Both compounds (III; R = Ph and Ph·CH_2) show general additional long-wavelength absorption, the

benzyl derivative exhibiting a shoulder at 2700 Å (ε *ca.* 400). The ultraviolet light absorption data for the 6-methyluracils (V) described in this and earlier work [2] are shown in Table 3; good general agreement with earlier data [6,7] on substituted uracils was found. The compounds (V) having R or R′ = Ph show a pronounced increase in ε at the position of minimum absorption (2350—2380 Å) over those uracils bearing non-aromatic

TABLE 4. *Oxazines* (II).[a]

	C=O str.	C=C str.	C=N str.	5C–H def.		
(II; R = R′ = *cyclo*hexyl)	1693	1646	*ca.* 1590	823	731	690
	(1320)	(800)	(*ca.* 10)	(250)	(28)	(55)
(II; R = R′ = Pr^i)	1692	1649	*ca.* 1590	823	731	690
	(1060)	(700)	(*ca.* 10)	(190)	(27)	(55)
(II; R = *cyclo*hexyl, R′ = Bu^t)	1693	1649	*ca.* 1590	824	733	692
	(1230)	(770)	(*ca.* 10)	(220)	(24)	(50)
(II; R = R′ = Et)	1692	1649	Not	823	729	689
	(1320)	(690)	detected	(180)	(20—25)[b]	(60)
(II; R = *cyclo*hexyl, R′ = C_8H_{17}[d])	1691	1645	*ca.* 1580	823	731	691
	(1300)	(800)	(*ca.* 10)	(230)	(25)	(55)
(II; R = Me, R′ = Ph)	1692	1649	1595	824	732	[b]
	(2100)	(990)	(400)	(280)	(25)	
(II; R = *cyclo*hexyl, R′ = Ph)	1690	1642	1594	825	730	[b]
	(1290)	(870)	(410)	(250)	(32)	
(II; R = Ph·CH_2, R′ = Ph)	1691	1651	1594	825	[b]	[b]
	(1670)	(740)	(410)	(210)		
(II; R = R′ = Ph)	1689	1650	1594	822[c]	[b]	[b]
	(1650)	(1070)	(450)			

[a] Carbon tetrachloride and *cyclo*hexane used as solvents (see Experimental section). [b] Interference from underlying bands. [c] Saturated solution used, concentration undetermined. [d] C_8H_{17} = 1 : 1 : 3 : 3-tetramethylbutyl.

TABLE 5. *Oxazines* (III).[a]

	2-oxo C=O str.	4-oxo C=O str.	C=C str.	5C–H def.	
(III; R = Me)[d]	1776	1711	1670	830	755
	(650)	(1320)	(50—100)	(200)	(310)
(III; R = Et)	1779	1712	1675	829	759
	(790)	(1620)	(50—100)	(190)	(230)
(III; R = Pr^i)	1779	1711	1672	829	761
	(650)	(1850)	(50—100)	(190)	(230)
(III; R = *cyclo*hexyl)[d]	1773	1711	1672	830	758
	(450)	(1350)	(50—100)	(160)	(250)
(III; R = Ph·CH_2)	1776	1711	1670	831	754
	(430)	(1150)	(50—100)	(200)	(260)
(III; R = Ph)[b]	1776	1721	1672	827	—[c]
	(—)	(—)	(—)	(—)	—

[a] Carbon tetrachloride and carbon disulphide used as solvents (see Experimental section). [b] Material sparingly soluble in solvents employed; saturated solutions used. [c] Interference from aromatic bands. [d] A 0·5 mm. cell was used.

substituents. This evidence and that afforded by infrared measurements (Table 6) confirm the structures proposed earlier [2] for (V; R = Me and Ph·CH_2, R′ = Ph).

The frequencies of infrared absorption maxima (see Tables 4—7) are measured in cm.$^{-1}$; the ε values are in parentheses and are approximate only. All three groups of compounds exhibit bands attributable to the C=O stretching frequency of the 4-oxo-grouping in conjugation with the C=C group (see Table 7); the dioxo-oxazines, however, show this band at about 1711 cm.$^{-1}$ rather than at the expected value of 1690—1695 cm.$^{-1}$ exhibited by the imino-oxazines (II), while the uracils show a band at about

[6] Evans, *J. Amer. Chem. Soc.*, 1952, **54**, 641.
[7] Austin, *ibid.*, 1934, **56**, 2141.

1670 cm.$^{-1}$. Compounds (III) and (V) show bands characteristic of the C=O stretching of the 2-oxo-group; the uracils show this band at about 1700 cm.$^{-1}$, whereas in the dioxo-oxazines the frequency is raised to 1775 cm.$^{-1}$, the C=O group in these compounds being part of a vinyl ester-like system. The imino-oxazines (II) show a C=N stretching band at 1590 cm.$^{-1}$ which is strong in intensity where R′ = Ph but only just observable where R′ is alkyl.

Table 7 shows the marked variations in both frequency and intensity exhibited by the stretching frequency of the C=C group conjugated with the 4-oxo-group. All three

TABLE 6. *6-Methyluracils.*[a]

		2-oxo C=O str.	4-oxo C=O str.	C=C str.	5C–H def.	
(V; R = R′ = Me)	(i)	1712	1675	1630	816	762
		(750)	(1500)	(250)	(240)	(230)
	(ii)	1700	1660	1621	847	766
		(750)	(1900)	(400)		
(V; R = R′ = Pr^{i})	(i)	1706	1670	1627	817	771
		(600)	(1800)	(200)	(210)	(220)
	(ii)	1694	1660	1616	823, 823	776
		(500)	(1800)	(250)		
(V; R = R′ = *cyclo*hexyl)	(i)	1706	1670	1627	815	768
		(650)	(2000)	(250)	(220)	(230)
	(ii)	1694	1656	1619	811, 820	772
		(500)	(1800)	(350)		
(V; R = Me, R′ = Ph·CH_2)	(i)	1705	1672	1626	818	765[b]
		(650)	(1900)	(200)	(250)	(190)
	(ii)	1697	1661	1624	874	767, 739, 735,
		(600)	(1800)	(300)	—	728, 694
(V; R = Me, R′ = Ph)	(i)	—[c]	1675	—	—	—
	(ii)	1703	1667	1626	848	769, 763, 703
		(650)	(1800)	(250)		
(V; R = Ph, R′ = Me)	(i)	—	—	—	—	—
	(ii)	1705	1667	1630	847	767, 753, 704
		(650)	(2100)	(shoulder)		693
(V; R = Ph·CH_2, R′ = Ph)	(i)	1705	1675	—	—	—
	(ii)	1703	1664	1624	847	774, 766, 763
		(600)	(1500)	(250)		711, 705, 669

[a] Series (i): carbon tetrachloride and carbon disulphide as solvents (see Experimental section). Series (ii): chloroform (1800—1600 cm.$^{-1}$), liquid paraffin mull (900—670 cm.$^{-1}$). The phenyl-substituted uracils were sparingly soluble in carbon tetrachloride. [b] Other bands due to the benzyl group were observed at 720 and 693 cm.$^{-1}$. [c] Where values for wave number are not quoted, bands were not of measurable intensity.

TABLE 7. *Light absorption (infrared) data* (CCl_4 *solutions*).

	4-oxo C=O str.		C=C str.	
	cm.$^{-1}$	ε	cm.$^{-1}$	ε
(II)[a]	1691—1693	1100—1300	1645—1649	700—800
(III)[b]	1711—1712	1300—1800	1664—1672	*ca.* 100
(V)[a]	1670—1675	1500—2000	1627—1630	200—250

[a] R and R′ are both aliphatic substituents. [b] R is aliphatic.

groups of compounds show bands of moderate intensity in the region 815—830 cm.$^{-1}$ which are attributed to the C–H deformation frequency of the grouping in the 5-position. Large variable frequency shifts were observed in the solid-phase spectra which were recorded for the uracils (Table 6, series ii) but the C–H deformation frequencies were clearly identifiable (underlined in the Table where two bands are quoted). No assignment can yet be offered for the bands exhibited in the 690—770 cm.$^{-1}$ range.

XUM

Experimental

M. p.s were determined on a Kofler block and are corrected.

p*K* values were obtained by titration of a 0·02M-solution in 50% v/v aqueous ethanol with 0·2N-sulphuric acid. A glass–calomel electrode system was used and an average of values given at 40%, 50%, and 60% complete neutralisation was taken. No corrections were imposed.

Ultraviolet-light absorptions refer to EtOH solutions. Infrared spectra were recorded by means of a Hilger H 800 double-beam instrument with a sodium chloride prism; carbon tetrachloride or chloroform (5000—850 cm.$^{-1}$), and *cyclo*hexane or carbon disulphide (850—670 cm.$^{-1}$), were used as solvents; the sample cell length was 0·1 mm.; frequencies are accurate to ± 3 cm.$^{-1}$ at 1700 cm.$^{-1}$ and ± 2 cm.$^{-1}$ at 820 cm.$^{-1}$.

3-cyclo*Hexyl*-2-cyclo*hexylimino*-2 : 3-*dihydro*-6-*methyl*-4-*oxo*-1 : 3-*oxazine* (II; R = R′ = *cyclo*hexyl).—Diketen (10·3 g.) was added during 0·5 hr. to a refluxing mixture of *NN′*-di*cyclo*hexylcarbodi-imide [8] (24 g.) and benzene (85 ml.), and the whole refluxed for a further 6 hr. Removal of the solvent gave a partly crystalline solid which on being rubbed with light petroleum (b. p. 60—80°) gave a solid (14·4 g.), m. p. 82°. Crystallisation from light petroleum (b. p. 60—80°) afforded the *oxazine* (II; R = R′ = *cyclo*hexyl) as prisms, m. p. 82—83° (lit.,[1] m. p. 82—83°) (Found: C, 70·4; H, 8·95; N, 9·7. $C_{17}H_{26}O_2N_2$ requires C, 70·3; H, 9·05; N, 9·65%).

This oxazine (5·00 g.) was refluxed with a mixture of concentrated hydrochloric acid (5 ml.) and water (50 ml.) for 1 hr. The solid dissolved but, after a few min., precipitation ensued. The precipitate (3·95 g.) was collected and extracted (Soxhlet) with hot light petroleum (b. p. 60—80°), to give (*a*) a residue (0·975 g.) insoluble in light petroleum, m. p. 233°, identified by mixed m. p. as *NN′*-di*cyclo*hexylurea (lit.,[9] m. p. 229—230°), (*b*) material (1·40 g.) soluble in hot light petroleum (b. p. 60—80°) but crystallising from it as plates, m. p. 178°, shown to be 3-cyclo*hexyl*-2 : 3-*dihydro*-6-*methyl*-2 : 4-*dioxo*-1 : 3-*oxazine* (III; R = *cyclo*hexyl) (Found: C, 62·85; H, 6·8; N, 6·8. $C_{11}H_{15}O_3N$ requires C, 63·15; H, 7·25; N, 6·7%), and (*c*) material (1·20 g.) soluble in cold light petroleum, which was separated from traces of (III; R = *cyclo*hexyl) by chromatography on alumina whence chloroform eluted 1 : 3-*di*cyclo*hexyl*-6-*methyluracil* (V; R = R′ = *cyclo*hexyl) which crystallised from aqueous methanol as plates, m. p. 137° (Found: C, 70·5; H, 8·85; N, 9·6. $C_{17}H_{26}O_2N_2$ requires C, 70·3; H, 9·05; N, 9·65%). The filtrate from the hydrolysis was shown, after the addition of alkali, to contain *cyclo*hexylamine by the reaction with *cyclo*hexyl *iso*thiocyanate to give *NN′*-di*cyclo*hexylthiourea, m. p. and mixed m. p. 188—189° (lit.,[9] m. p. 180—181°).

The oxazine (III; R = *cyclo*hexyl) (0·5 g.) was heated at 60—70° with ethanol (10 ml.) and aqueous ammonia (*d* 0·88; 10 ml.) for 2 hr. The mixture was evaporated to dryness; the residue, crystallised from ethyl acetate–light petroleum (b. p. 60—80°), gave 3-cyclo*hexyl*-6-*methyluracil*, needles, m. p. 238·5—239° (Found: C, 62·9; H, 7·25; N, 12·9. $C_{11}H_{16}O_2N_2$ requires C, 63·45; H, 7·75; N, 13·45%).

2 : 3-*Dihydro*-6-*methyl*-4-*oxo*-3-iso*propyl*-2-iso*propylimino*-1 : 3-*oxazine* (II; R = R′ = Pr^i).—Prepared according to the previous method from *NN′*-di*iso*propylcarbodi-imide [10] (22·7 g.) and diketen (16·8 g.) in benzene (60 ml.), the *oxazine* (II; R = R′ = Pr^i) (32·7 g.) had b. p. 89—92°/1·5 mm., m. p. 30° (prisms) (lit.,[1] b. p. 80—82°/0·5 mm., m. p. 32°) (Found: N, 13·5. $C_{11}H_{18}O_2N_2$ requires N, 13·3%).

This oxazine (12·0 g.) was refluxed with concentrated hydrochloric acid (12 ml.) and water (120 ml.), an oil being deposited. Isolation with ether gave an oil (8·4 g.) from which, after addition of light petroleum (b. p. 40—60°), a solid (0·2 g.), m. p. 200°, identified by mixed m. p. as *NN′*-di-*iso*propylurea (lit.,[11] m. p. 192°), was deposited. Evaporation of the filtrate gave a solid which crystallised as sharp-melting prisms, m. p. 44—45°, but nevertheless, was shown by infrared analysis to be a mixture of (III; R = Pr^i) (54%) and (V; R = R′ = Pr^i) (44%). The mixture was chromatographed on alumina; elution with light petroleum (b. p. 40—60°)–benzene and crystallisation from light petroleum (b. p. 60—80°) gave 2 : 3-*dihydro*-6-*methyl*-2 : 4-*dioxo*-3-iso*propyl*-1 : 3-*oxazine* (III; R = Pr^i), prisms, m. p. 62·5—63° (Found: C, 56·5;

[8] Schmidt, Hitzler, and Lahde, *Ber.*, 1938, **71**, 1933.
[9] Skita and Rolfes, *Ber.*, 1920, **53**, 1242.
[10] Schmidt and Striewsky, *Ber.*, 1941, **74**, 1285.
[11] Hofmann, *Ber.*, 1882, **15**, 752.

XUM

H, 6·3; N, 8·15. $C_8H_{11}O_2N$ requires C, 56·8; H, 6·55; N, 8·3%). Elution with benzene–chloroform and crystallisation from water gave 6-*methyl*-1 : 3-*di*iso*propyluracil* (V; R = R′ = Pr^i), needles, m. p. 93—94° (Found: C, 62·75; H, 8·2; N, 13·2. $C_{11}H_{18}O_2N_2$ requires C, 62·8; H, 8·65; N, 13·3%).

The aqueous layer from the hydrolysis was made alkaline and distilled; titration of the distillate showed it to contain 44% of the amine theoretically obtainable by conversion of (II; R = R′ = Pr^i) into (III; R = Pr^i).

The oxazine (III; R = Pr^i) (0·5 g.) was heated in a boiling-water bath with aqueous ammonia (*d* 0·880; 10 ml.) for 1 hr. Evaporation and crystallisation of the residue from ethyl acetate–light petroleum (b. p. 60—80°) gave 6-*methyl*-3-iso*propyluracil* (V; R = Pr^i, R′ = H) as needles, m. p. 193° (Found: C, 57·3; H, 7·2; N, 16·5. $C_8H_{12}O_2N_2$ requires C, 57·15; H, 7·2; N, 16·65%).

3-*Ethyl*-2-*ethylimino*-2 : 3-*dihydro*-6-*methyl*-4-*oxo*-1 : 3-*oxazine* (II; R = R′ = Et).—*NN*′-Diethylcarbodi-imide [9] (9·1 g.; b. p. 71—72°/100 mm.; lit.,[12] b. p. 24·5°/11 mm.) with diketen (8·5 g.) in benzene (30 ml.) gave the oxazine (II; R = R′ = Et) (15·1 g.), b. p. 82°/1 mm., n_D^{20} 1·4996. The identity of the product was established by comparison of the infrared spectrum with that of an authentic specimen and acid hydrolysis to compound (III; R = Et), m. p. and mixed m. p. 71° (lit.,[3] m. p. 69—70°).

2-tert.-*Butylimino*-3-cyclo*hexyl*-2 : 3-*dihydro*-6-*methyl*-4-*oxo*-1 : 3-*oxazine* (II; R = *cyclo*hexyl, R′ = Bu^t). The *oxazine* was obtained by the standard procedure from *N*-*tert.*-butyl-*N*′-*cyclo*hexylcarbodi-imide [13] (25 g.) and diketen (12·5 g.) in benzene (40 ml.) as an oil (29·8 g.), b. p. 134—137°/1·5 mm., needles, m. p. 69° (from aqueous methanol) (lit.,[1] m. p. 58—60°) (Found: C, 67·9; H, 9·0; N, 10·9. $C_{15}H_{24}O_2N_2$ requires C, 68·15; H, 9·15; N, 10·6%).

This oxazine (2·0 g.) was refluxed with concentrated hydrochloric acid (2 ml.) and water (20 ml.) for 1 hr. After cooling, the product (0·87 g.; m. p. 167°) was collected and crystallised from light petroleum (b. p. 80—100°), giving compound (III; R = *cyclo*hexyl), m. p. and mixed m. p. 178°. The filtrate was concentrated to small bulk and made alkaline; the precipitate (0·39 g.; m. p. 197°), recrystallised from ethyl acetate, gave *cyclo*hexylurea as plates, m. p. and mixed m. p. 199° (lit.,[14] m. p. 195—196°). Experiments with more concentrated acid gave lower yields of (III; R = *cyclo*hexyl) and higher yields of *cyclo*hexylurea. Hydrolysis of the oxazine (2·0 g.) with concentrated hydrochloric acid (4 ml.) gave only a trace of (III; R = *cyclo*hexyl), and 0·76 g. of *cyclo*hexylurea. When concentrated hydrochloric acid (0·5 ml.) and water (4·5 ml.) were used, *cyclo*hexylurea (0·08 g.) and a mixture of non-basic solids (1·29 g.) were obtained; the latter was resolved by Soxhlet extraction with light petroleum (b. p. 60—80°) into (III; R = *cyclo*hexyl) (0·47 g.) and a residue (0·49 g.) which, on crystallisation from aqueous ethanol, gave N-tert.-*butyl*-N′-cyclo*hexylurea* as needles, m. p. and mixed m. p. 227° (Found: C, 66·9; H, 11·15; N, 13·7. $C_{11}H_{22}ON_2$ requires C, 66·6; H, 11·15; N, 14·15%).

An authentic specimen of *N*-*tert.*-butyl-*N*′-*cyclo*hexylurea was prepared by refluxing *N*-*tert.*-butyl-*N*′-*cyclo*hexylcarbodi-imide (4 g.) with concentrated hydrochloric acid (0·5 ml.) and water (10 ml.) for 10 min., to give a solid (3·9 g.) which crystallised from aqueous ethanol as needles, m. p. 227°. Hydrolysis of the urea (1·0 g.) in boiling concentrated hydrochloric acid (2 ml.) and water (2 ml.) for 1 hr. gave, after concentration and addition of alkali, *cyclo*hexylurea (0·60 g., 85%), m. p. and mixed m. p. 197°.

N-cyclo*Hexyl*-N′-1 : 1 : 3 : 3-*tetramethylbutylthiourea*.—*cyclo*Hexyl *iso*thiocyanate (28 g.) was added during 0·5 hr. to 2-amino-2 : 4 : 4-trimethylpentane (26 g.; redistilled; b. p. 140—140·5°) in boiling light petroleum (b. p. 40—60°; 100 ml.), and the mixture was refluxed for 2 hr. The *thiourea* (45·6 g.; m. p. 123—125°) was collected; it formed needles, m. p. 125°, from light petroleum (b. p. 80—100°) (Found: N, 10·05. $C_{15}H_{30}N_2S$ requires N, 10·35%).

N-cyclo-*Hexyl*-N′-1 : 1 : 3 : 3-*tetramethylbutylcarbodi-imide*.—Prepared by the standard method of Schmidt *et al.*, the *carbodi-imide* was obtained in 81% yield as an oil 110—112°/1·5 mm., n_D^{20} 1·4835 (Found: C, 76·4; H, 12·0; N, 11·8. $C_{15}H_{28}N_2$ requires C, 76·2; H, 11·95; N, 11·85%).

3-cyclo*Hexyl*-2 : 3-*dihydro*-6-*methyl*-4-*oxo*-2-(1 : 1 : 3 : 3-*tetramethylbutyl*)*imino*-1 : 3-*oxazine* (II; R = *cyclo*hexyl, R′ = 1 : 1 : 3 : 3-tetramethylbutyl).—*N*-*cyclo*Hexyl-*N*′-1 : 1 : 3 : 3-tetramethylbutylcarbodi-imide (15 g.), diketen (6 g.), and benzene (20 ml.) were refluxed for 6 hr. Isolation gave a semi-solid fraction (15 g.), b. p. 140—158°/1·5 mm., a portion (3·4 g.) of which

[12] Staudinger and Hauser, *Helv. Chim. Acta*, 1922, **4**, 861.
[13] Schmidt, Striewsky, and Hitzler, *Annalen*, 1948, **560**, 222.
[14] Wallach, *Annalen*, 1905, **343**, 46.

XUM

was separated by chromatography on alumina to give, (*a*) by elution with benzene–light petroleum (b. p. 40—60°) the *oxazine* (II; R = *cyclo*hexyl, R′ = 1 : 1 : 3 : 3-tetramethylbutyl) (2·4 g.) which crystallised as needles, m. p. 59·5—60° (lit.,[1] m. p. 59—60°), from aqueous methanol (Found: C, 71·5; H, 10·15; N, 8·65. $C_{19}H_{32}O_2N_2$ requires C, 71·2; H, 10·05; N, 8·75%), and (*b*) by elution with ether *N-cyclo*hexyl-*N*′-1 : 1 : 3 : 3-tetramethylbutylurea (0·6 g.), m. p. and mixed m. p. 158—159°. An authentic sample was prepared by the action of hot dilute hydrochloric acid on the di-imide (I; R = *cyclo*hexyl, R′ = 1 : 1 : 3 : 3-tetramethylbutyl); the *urea* crystallised from aqueous ethanol as needles, m. p. 160·5° (Found: N, 10·7. $C_{15}H_{30}ON_2$ requires N, 11·0%).

The oxazine (II; R = *cyclo*hexyl, R′ = 1 : 1 : 3 : 3-tetramethylbutyl) (0·5 g.) was refluxed with concentrated hydrochloric acid (1 ml.) and water (1 ml.) for 1 hr. Filtration of the cooled product afforded compound (III; R = *cyclo*hexyl), m. p. and mixed m. p. 177—178°, and concentration and basification of the filtrate gave a solid (0·30 g.), m. p. 187—188°, which, on crystallisation from ethyl acetate gave *cyclo*hexylurea, m. p. and mixed m. p. 198°. Hydrolysis of compound (IV; R = *cyclo*hexyl, R′ = 1 : 1 : 3 : 3-tetramethylbutyl) under similar conditions gave *cyclo*hexylurea in high yield.

3-cyclo*Hexyl*-2 : 3-*dihydro*-6-*methyl*-4-*oxo*-2-*phenylimino*-1 : 3-*oxazine* (II; R = *cyclo*hexyl, R′ = Ph).—A mixture of *N-cyclo*hexyl-*N*′-phenylcarbodi-imide [5] (11·0 g.), diketen (5 g.), benzene (30 ml.), and cuprous chloride (0·1 g.) was refluxed for 6 hr. Isolation and distillation afforded a viscous oil (8·0 g.), b. p. 165—195°/2 mm., which crystallised; crystallisation from aqueous methanol afforded the *oxazine* as prisms, m. p. 109·5° (Found: C, 72·1; H, 7·15; N, 9·8. $C_{17}H_{20}O_2N_2$ requires C, 71·8; H, 7·1; N, 9·85%). From a similar preparation without the cuprous chloride, the carbodi-imide was recovered with 80% efficiency.

The oxazine was refluxed with concentrated hydrochloric acid (1 ml.) and water (10 ml.) for 1·5 hr. and the product was crystallised from aqueous methanol, to give compound (III; R = *cyclo*hexyl) (0·19 g.), m. p. and mixed m. p. 176—177°. Addition of water to the mother-liquors gave a precipitate which recrystallised from benzene–light petroleum (b. p. 60—80°) as prisms, m. p. 192°, undepressed on admixture with authentic *N-cyclo*hexyl-*N*′-phenylurea (lit.,[9] m. p. 182°).

2 : 3-*Dihydro*-6-*methyl*-4-*oxo*-3-*phenyl*-2-*phenylimino*-1 : 3-*oxazine* (II; R = R′ = Ph).—A mixture of *NN*′-diphenylcarbodi-imide (19·4 g.), diketen (9 g.), benzene (50 ml.), and cuprous chloride (0·1 g.) was refluxed for 8 hr. Filtration and removal of solvents gave a dark glass from which, by rubbing with methanol, a brown solid (8·0 g.), m. p. 155—165°, was isolated. Crystallisation from ethyl acetate–light petroleum (b. p. 60—80°) gave the oxazine (II; R = R′ = Ph) as prisms, m. p. and mixed m. p. 182—183° (lit.,[2] m. p. 184—185°).

Reaction of N-*Benzyl*-N′-*phenylcarbodi-imide with Diketen.*—This *carbodi-imide* was prepared by the standard method of Schmidt and Striewsky [10] in 54% yield as an oil, b. p. 148—152°/2·5 mm., n_D^{20} 1·6118 (Found: N, 13·6. $C_{14}H_{12}N_2$ requires N, 13·45%). The preparation was remarkably difficult to reproduce. A mixture of the carbodi-imide (15·6 g.), diketen (6·5 g.), benzene (20 ml.), and toluene-*p*-sulphonic acid (0·1 g.) was refluxed for 6 hr. Distillation afforded a semi-solid fraction, b. p. 200—225°/2 mm., from which, by rubbing with methanol, 1-benzyl-6-methyl-3-phenyluracil (3·0 g.), m. p. and mixed m. p. 223—224° (lit.,[2] m. p. 226—227°), was isolated.

We thank the management of this division of the Distillers Co. Ltd. for permission to publish this paper.

BRITISH INDUSTRIAL SOLVENTS, DEVELOPMENT DEPARTMENT,
HEDON, HULL. [*Received, December 31st*, 1957.]

XUM

438. *Bisbenzylisoquinolines. Part II.*[1] *The Synthesis of 5-(2-Aminoethyl)-4′-carboxy-2 : 3-dimethoxydiphenyl Ether.*

By J. R. Crowder, M. F. Grundon, and J. R. Lewis.

The preparation of diphenyl ether derivatives from methyl 4-chloro-3 : 5-dinitrobenzoate, and from methyl 4-chloro-3-nitrobenzoate, and phenols has been examined. Both reactions lead to syntheses of the amino-acid (I) and its *N*-phthaloyl derivative.

The amino-acid (I) was required as an intermediate in a synthesis of bisbenzyl*iso*quinoline alkaloids of the tubocurarine type. A major difficulty in the preparation of these compounds lies in the formation of the diphenyl ether system, as was shown in the synthesis[1] of the related amino-acid (II). The latter compound was prepared by condensation of 4-chloro-3-methoxy-5-nitrobenzaldehyde with methyl 3-hydroxy-4-methoxyphenylacetate in pyridine, subsequent stages involving reduction, deamination, and conversion of the formyl group into a 2-aminoethyl side-chain.

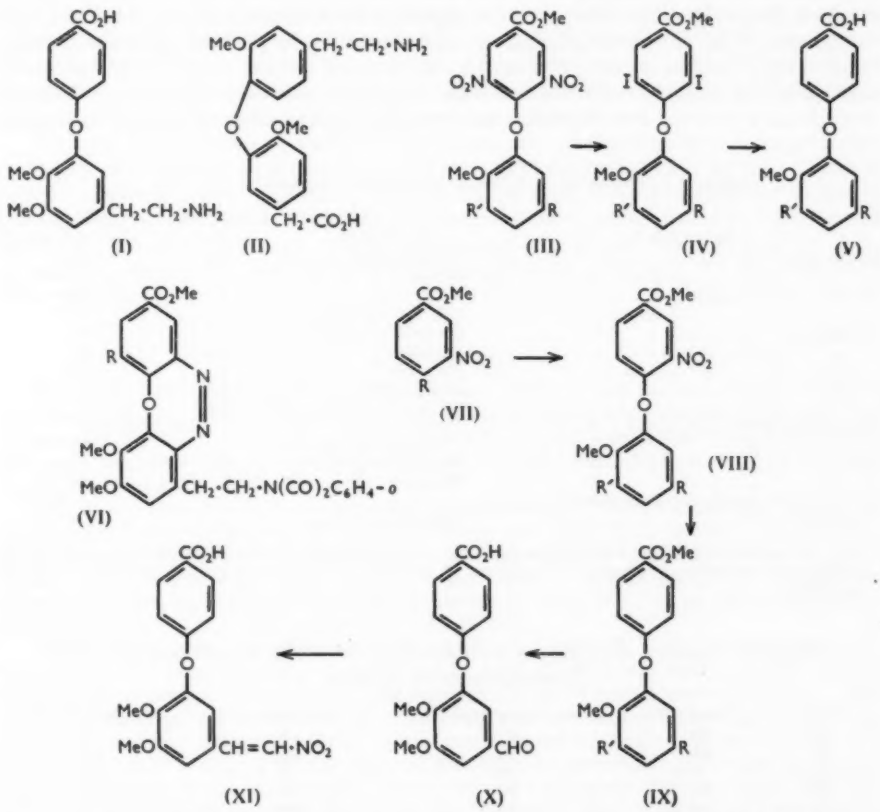
A similar scheme was envisaged for the amino-acid (I), but in this case the presence of an aromatic ring without methoxyl groups allows the use of a triply activated halogenobenzene in the condensation with a suitable phenol. Methyl 4-chloro-3 : 5-dinitrobenzoate has been shown[2] to give diaryl ethers readily, and, in a preliminary experiment, the chloro-compound and guaiacol in pyridine at room temperature afforded the diphenyl ether derivative (III; R = R′ = H) in 80% yield. Reduction to the corresponding diamine proceeded normally as shown by the isolation of a diacetyl derivative (95%), but tetrazotisation of the amine in aqueous solution or with nitrosylsulphuric acid, followed by treatment with hypophosphorous acid, gave no characterisable product. Hems and his co-workers[3] converted numerous dinitrodiphenyl ethers into the corresponding di-iodo-derivatives, and application of their method to our diamine gave the di-iodo-compound (IV; R = R′ = H) (21%). Catalytic reduction in the presence of diethylamine afforded methyl 4-*o*-methoxyphenoxybenzoate in high yield. The corresponding acid (V; R = R′ = H), obtained by hydrolysis, was prepared by Ungnade[4] by a different method.

The moderate success of this scheme encouraged its application to the synthesis of the amino-acid (I). 2 : 3-Dimethoxy-5-2′-phthalimidoethylphenol was chosen for the initial condensation. An essential intermediate in the synthesis of this phenol, namely, 3-hydroxy-4 : 5-dimethoxybenzaldehyde, was conveniently prepared by the McFadyen-Stephens method, as an alternative to other processes.[5,6] Späth and Roder[6] converted 3-ethoxycarbonyloxy-4 : 5-dimethoxybenzaldehyde into the nitrovinyl derivative, which, on reduction and hydrolysis, furnished 2 : 3-dimethoxy-5-2′-aminoethylphenol: we obtained 2 : 3-dimethoxy-5-2′-phthalimidoethylphenol from 3-hydroxy-4 : 5-dimethoxybenzaldehyde in 61% yield *via* the nitrovinyl derivative, without purification of the intermediate amine. Condensation with methyl 4-chloro-3 : 5-dinitrobenzoate then gave the diphenyl ether [III; R = $CH_2{\cdot}CH_2{\cdot}N(CO)_2C_6H_4$-*o*, R′ = OMe] (90%), which was reduced to an unstable diamine, characterised as its diacetate. Tetrazotisation of the crude diamine, followed by reaction with sodium iodide and iodine, gave a difficultly separable mixture of the colourless di-iododiphenyl ether [IV; R = $CH_2{\cdot}CH_2{\cdot}N(CO)_2C_6H_4$-*o*, R′ = OMe] (20—40%) and an orange compound (10—40%), $C_{28}H_{20}O_7N_2I$, considered to be the dibenzoxadiazepine (VI; R = I). The extended conjugation in the latter is shown

[1] Part I, Grundon and Perry, *J.*, 1954, 3531.
[2] Borrows, Clayton, Hems, and Long, *J.*, 1949, S190.
[3] Borrows, Clayton, and Hems, *J.*, 1949, S185; Chalmers, Dickson, Elk, and Hems, *J.*, 1949, **3424**.
[4] Ungnade, *J. Amer. Chem. Soc.*, 1941, **63**, 2091.
[5] Mauthner, *Annalen*, 1926, **449**, 102.
[6] Späth and Roder, *Monatsh.*, 1922, **43**, 93.

by the ultraviolet spectrum ($\lambda_{max.}$ 360 mμ; log ε 3·8) which contrasts with that of the di-iodo-compound [IV; R = $CH_2{\cdot}CH_2{\cdot}N(CO)_2C_6H_4$-*o*, R′ = OMe] (no intense absorption above 270 mμ). The iododibenzoxadiazepine, on catalytic reduction, gave the dibenzoxadiazepine (VI; R = H) ($\lambda_{max.}$ 360 mμ, log ε 3·7) quantitatively. The iododibenzoxadiazepine is formed apparently by an azo-coupling reaction, for which the intermediate tetrazonium salt is particularly suitable in that *m*-tetrazonium compounds are known to couple in strongly acid solution,[7] there is a free position *para* to a methoxyl group in the other aromatic ring, and the remaining substituents in this ring are situated favourably. Dibenz-1 : 4 : 5-oxadiazepines have not been recorded previously.

Catalytic reduction of the di-iodo-derivative [IV; R = $CH_2{\cdot}CH_2{\cdot}N(CO)_2C_6H_4$-*o*, R′ = OMe] gave a product which did not crystallise and, without purification, was



hydrolysed with potassium hydrogen carbonate. As this process is liable to open the phthalimido-ring, the crude acid was heated at 150° to effect ring closure to the *N*-phthalimido-acid [V; R = $CH_2{\cdot}CH_2{\cdot}N(CO)_2C_6H_4$-*o*, R′ = OMe] (27%).

The overall yield (6%, based on 3-hydroxy-4 : 5-dimethoxybenzaldehyde) in this synthesis is not satisfactory, and the deamination stage is not reliable. Consequently, a second route (VII—XI) to the amino-acid (I) and its *N*-phthaloyl derivative was explored, using the mononitro-esters (VII; R = Cl, F, or $O{\cdot}SO_2{\cdot}C_6H_4Me$-*p*). Analogous

[7] Schoutissen, *Rec. Trav. chim.*, 1935, **54**, 381.

halogenobenzenes, such as 1-chloro-2 : 4-dinitrobenzene and 4-chloro-3-methoxy-5-nitrobenzaldehyde, require elevated temperatures for condensation with phenols in pyridine.[1,2] Borrows *et al.*[2] showed that excess of the phenolic component increased the yield of diphenyl ether, but in all our studies we used equimolecular quantities of phenol and halogenobenzene, because the phenol is often difficult of access. Methyl 4-chloro-3-nitrobenzoate and guaiacol gave the diphenyl ether derivative (VIII; R = R′ = H) (51%), but 2 : 3-dimethoxy-5-2′-phthalimidoethylphenol gave no diphenyl ether although none of the phenol was recovered. Thus, the *N*-phthaloyl group appears to be unstable to boiling pyridine, and phenolic aldehydes were employed in subsequent studies.

*iso*Vanillin and methyl 4-chloro-3-nitrobenzoate afforded the diphenyl ether derivative (VIII; R = CHO, R′ = H) (50—60%) with pyridine or with potassium carbonate, whereas use of the potassium derivative of *iso*vanillin in dimethylformamide or in diethylene glycol dimethyl ether gave the diphenyl ether in lower yield. The toluene-*p*-sulphonate (VII; R = O·SO_2·C_6H_4Me-*p*) and *iso*vanillin in pyridine gave the diphenyl ether (55%), but in dimethylformamide or in ethyl methyl ketone with potassium carbonate the only product isolated was *iso*vanillin toluene-*p*-sulphonate. Although there is some evidence that fluorine is more readily displaced than chlorine in nucleophilic

TABLE 1. *Preparation of the diphenyl ether derivatives* (VIII).

Reactants [a]	Conditions	Reflux time (hr.)	Yield (%) of diphenyl ether
*iso*Vanillin + A	$COMeEt–K_2CO_3$	1·5	60 [c]
,, + A	Pyridine	1	55 [b]
K deriv. of *iso*vanillin + A	NMe_2·CHO	2	25 [c]
,, + A	$O(CH_2·CH_2·OMe)_2$	1	30 [b]
*iso*Vanillin + B	$COMeEt–K_2CO_3$	1·5	55 [c]
,, + B	Pyridine	1·5	60 [b]
,, + C	Pyridine	1	55 [b]
,, + C	NMe_2·CHO	0·5	0
,, + C	$O(CH_2·CH_2·OMe)_2$	2·5	0
3 : 4 : 5-$HO(MeO)_2C_6H_2$·CHO + A	Pyridine	(see Table 2)	
,, + A	$COMeEt–K_2CO_3$	1	25 [b]
,, + B	$COMeEt–K_2CO_3$	1	35 [b]
,, + C	Pyridine	1	30 [c]
K deriv. of 3-hydroxy-4 : 5-dimethoxybenzaldehyde + A	$O(CH_2·CH_2·OMe)_2$	1	30 [c]

[a] A = Methyl 4-chloro-3-nitrobenzoate. B = Methyl 4-fluoro-3-nitrobenzoate. C = 4-Methoxycarbonyl-2-nitrophenyl toluene-*p*-sulphonate. [c] Isolated by crystallisation. [b] Isolated by chromatography.

TABLE 2. *Reaction of 3-hydroxy-4 : 5-dimethoxybenzaldehyde with methyl 4-chloro-3-nitrobenzoate in pyridine.*

Temp.	Time (hr.)	Phenol recovered (%)	Diphenyl ether (%)	By-product (%)
25°	20	50	0	0
75	66	40	25	—
85	2·5	30	5	10
80	60	50	25	20
114	0·25	75	20	8
114	0·5	70	20	15
114	1	25	30	35

reactions with activated halogenobenzenes,[3] methyl 4-fluoro-3-nitrobenzoate showed reactivity similar to that of the chloro-compound when condensed with *iso*vanillin. Parallel reactions were carried out with 3-hydroxy-4 : 5-dimethoxybenzaldehyde, giving the diphenyl ether derivative (VIII; R = CHO, R′ = OMe) (25—33%), and the results

[3] Cf. Bunnett and Zahler, *Chem. Rev.*, 1951, **49**, 273.

for both phenols are incorporated in Table 1. The reaction of 3-hydroxy-4 : 5-dimethoxybenzaldehyde and methyl 4-chloro-3-nitrobenzoate in pyridine was studied in detail (Table 2). More vigorous conditions increased the yield of diphenyl ether, but the amount of phenol recovered was much less, apparently because of the increased production of a by-product which did not crystallise and was not investigated. The by-product was not detected in the preparation of the diphenyl ether (70%, based on phenol used) from methyl 4-chloro-3-nitrobenzoate and the potassium salt of the phenol in diethylene glycol dimethyl ether, and this method proved convenient for large-scale reactions.

The nitrodiphenyl ether (VIII; R = R′ = H) was reduced almost quantitatively to the amine, which on diazotisation and reduction of the diazonium salt with hypophosphorous acid afforded the diphenyl ether derivative (IX; R = R′ = H) (43%), identical with the compound prepared from the dinitrodiphenyl ether, as described above. Reduction and deamination of the nitrodiphenyl ether derivatives (VIII; R = CHO, R′ = H and OMe), after protection of the formyl groups by acetylation, furnished the diphenyl ethers (IX; R = CHO, R′ = H) (45%) and (IX; R = CHO, R′ = OMe) (70%), without purification of the intermediate amines. Isolation of the diazofluoroborates, followed by reduction by Roe and Graham's method,[9] was not advantageous.

The acid (X), obtained in good yield by hydrolysis of its methyl ester with potassium hydrogen carbonate, was converted into its nitrovinyl derivative (XI) (63%). Catalytic reduction afforded the required amino-acid (I), isolated more conveniently as its *N*-phthaloyl derivative (43%), identical with the compound prepared earlier. The overall yield (11%, from 3-hydroxy-4 : 5-dimethoxybenzaldehyde), and the convenience of the operations, compared favourably with the alternative route through the dinitrodiphenyl ether derivatives.

Experimental

Methyl 4-o-*Methoxyphenoxy*-3 : 5-*dinitrobenzoate* (III; R = R′ = H).—Methyl 4-chloro-3 : 5-dinitrobenzoate (1·3 g.) was shaken with guaiacol (0·62 g.) in pyridine (8 c.c.) at room temperature for 30 hr. Addition of water gave the *diphenyl ether*, crystallising from ethanol (charcoal) in yellow needles (1·39 g., 80%), m. p. 134—136° (Found: C, 51·9; H, 3·6. $C_{15}H_{12}O_8N_2$ requires C, 51·7; H, 3·5%).

Methyl 3 : 5-*Diacetamido*-4-o-*methoxyphenoxybenzoate*.—The dinitro-compound (0·56 g.) in ethyl acetate was hydrogenated at room temperature and atmospheric pressure with platinum. Removal of the catalyst and the solvent gave the diamine, m. p. 176—191°, which darkened rapidly. Acetylation with acetic anhydride and aqueous sodium hydroxide afforded the *diacetyl derivative*, separating from ethanol in needles (0·58 g., 95%), m. p. 236—238° (Found: C, 61·2; H, 5·4. $C_{19}H_{20}O_6N_2$ requires C, 61·3; H, 5·4%).

Methyl 3 : 5-*Di-iodo*-4-o-*methoxyphenoxybenzoate* (IV; R = R′ = H).—Methyl 4-o-methoxyphenoxy-3 : 5-dinitrobenzoate (2 g.) in acetic acid (15 c.c.) was hydrogenated at room temperature and atmospheric pressure with platinum (0·2 g.) (6 mols. absorbed in 1 hr.). After removal of the catalyst, the solution was added during 40 min. to a stirred solution of nitrosylsulphuric acid [from sodium nitrite (1 g.) and concentrated sulphuric acid (20 c.c.)] in acetic acid (15 c.c.) at 0°. After 1 hr., the mixture was added in portions during 5 min. to a stirred mixture of sodium iodide (4 g.), iodine (3·4 g.), urea (0·5 g.), water (260 c.c.), and chloroform (50 c.c.). The solution was kept for 1½ hr., the chloroform was separated, and the aqueous solution and the tarry residue were washed with chloroform. The combined chloroform solution was washed with aqueous sodium sulphite saturated with sulphur dioxide, and with water, and then evaporated. The residue, in acetone, was added to an alumina column. Elution with acetone and evaporation of the solvent gave a solid residue. Crystallisation from ethanol afforded the *di-iodo-compound* as needles (0·67 g., 21%), m. p. 131—135° (Found: C, 35·6; H, 2·6; I, 49·6. $C_{15}H_{12}O_4I_2$ requires C, 35·4; H, 2·4; I, 49·9%).

Methyl 4-o-*Methoxyphenoxybenzoate*.—(*a*) Methyl 3 : 5-di-iodo-4-*o*-methoxyphenoxybenzoate (0·5 g.) and diethylamine (0·2 g.) in ethyl acetate were hydrogenated at room temperature

[9] Roe and Graham, *J. Amer. Chem. Soc.*, 1952, **74**, 6297.

and atmospheric pressure in the presence of platinum. The filtered solution was washed with dilute hydrochloric acid, and with water, and evaporated. Distillation of the residue gave *methyl* 4-*o*-*methoxyphenoxybenzoate*, b. p. 154° (bath)/0·5 mm., separating from ethanol in prisms (0·22 g., 80%), m. p. 66—67° (Found: C, 69·8; H, 5·3. $C_{15}H_{14}O_4$ requires C, 69·8; H, 5·5%).

The corresponding acid, obtained by hydrolysis with potassium hydrogen carbonate in aqueous methanol, crystallised from light petroleum (b. p. 80—100°) in prisms, m. p. 156—157° (lit.,[4] 159°).

(*b*) Methyl 3-amino-4-*o*-methoxyphenoxybenzoate (see below) (0·5 g.) in 20% hydrochloric acid (15 c.c.) was diazotised at −5° with sodium nitrite (0·2 g.). After addition of 30% aqueous hypophosphorous acid (15 c.c.), the solution was kept at 0° for 12 hr. and extracted with ether. Evaporation of the ether and distillation of the residue gave methyl 4-*o*-methoxyphenoxybenzoate, b. p. 100° (bath)/0·01 mm. (0·21 g., 43%), m. p. or mixed m. p. 67°.

N-*Benzenesulphonyl*-N′-4 : 5-*dimethoxy*-3-*methoxycarbonyloxybenzoylhydrazine*.—4 : 5-Dimethoxy-3-methoxycarbonyloxybenzoyl chloride (4·2 g.) in benzene was added in portions to benzenesulphonhydrazide (2·9 g.) in pyridine (10 c.c.). The solution was stirred for 1 hr. and poured into dilute hydrochloric acid at 0°, and the precipitate collected and combined with a further quantity obtained by separation and concentration of the organic layer. Crystallisation from ethanol afforded the *diacylhydrazine* in prisms (4·3 g., 75%), m. p. 166—169° (Found: C, 49·5; H, 4·6. $C_{17}H_{18}O_8N_2S$ requires C, 49·7; H, 4·4%).

3-*Hydroxy*-4 : 5-*dimethoxybenzaldehyde*.—Anhydrous sodium carbonate (6·2 g.) was added in one portion to a solution of the diacylhydrazine (5 g.) in ethylene glycol (70 c.c.) at 160° (internal temp.). After 75 sec., water (500 c.c.) was added, and the solution was acidified with dilute sulphuric acid and extracted with ether (6 × 30 c.c.). The ether solution was washed with aqueous sodium hydrogen carbonate and with water, and evaporated. Distillation of the residue at 0·5 mm. gave the aldehyde (1·74 g., 70%), b. p. 150—155°, needles [from light petroleum (b. p. 60—80°)], m. p. 59—60° (lit.,[5] m. p. 60—61°) (Found: C, 59·1; H, 5·6. Calc. for $C_9H_{10}O_4$: C, 59·3; H, 5·5%). The 2 : 4-*dinitrophenylhydrazone* separated from acetic acid in red needles, m. p. 264—265° (Found: C, 49·8; H, 4·1. $C_{15}H_{14}O_7N_4$ requires C, 49·8; H, 3·9%).

3-*Hydroxy*-4 : 5-*dimethoxy*-ω-*nitrostyrene*.—A mixture of 3-hydroxy-4 : 5-dimethoxybenzaldehyde (4·7 g.), nitromethane (5 c.c.), ammonium acetate (2 g.), and acetic acid (20 c.c.) was heated under reflux for 2 hr., and added to water. The precipitate, on crystallisation from ethanol, gave the *nitrostyrene derivative* (4·07 g., 69%), m. p. 160—170°, recrystallising in yellow needles, m. p. 168—170° (Found: C, 53·6; H, 5·1. $C_{10}H_{11}O_5N$ requires C, 53·4; H, 4·9%).

2 : 3-*Dimethoxy*-5-2′-*phthalimidoethylphenol*.—The nitrostyrene derivative (0·61 g.) in ethyl acetate was added to platinum oxide prereduced in 10% aqueous sulphuric acid (6 c.c.), and hydrogenated at room temperature and atmospheric pressure until 4 mol. of hydrogen had been absorbed (1 hr.). After removal of the catalyst the aqueous layer was separated, and the ethyl acetate solution washed with water. The combined aqueous solution was passed through an ion-exchange column (Amberlite IR-4B), and the eluate was evaporated. The residue in acetic acid was heated under reflux with phthalic anhydride (0·48 g.) for 30 min. Addition of water gave a precipitate of the *phthalimidophenol* (0·72 g., 91%), crystallising from ethanol in prisms, m. p. 219—221° (Found: C, 66·0; H, 5·5. $C_{18}H_{17}O_5N$ requires C, 66·0; H, 5·2%).

Methyl 4-(2 : 3-*Dimethoxy*-5-2′-*phthalimidoethylphenoxy*)-3 : 5-*dinitrobenzoate* [III; R = $CH_2{\cdot}CH_2{\cdot}N(CO)_2C_6H_4$-*o*, R′ = OMe].—2 : 3-Dimethoxy-5-2′-phthalimidoethylphenol (0·146 g.), methyl 4-chloro-3 : 5-dinitrobenzoate (0·176 g.), and pyridine (10 c.c.) were kept at room temperature for 36 hr., chloroform was added, and the solution washed with dilute hydrochloric acid, N-aqueous sodium hydroxide, and water. Evaporation and crystallisation of the residue from ethanol gave the *diphenyl ether* as yellow plates (0·22 g., 90%), m. p. 184—186° (Found: C, 56·5; H, 3·6; N, 7·6. $C_{26}H_{21}O_{11}N_3$ requires C, 56·6; H, 3·8; N, 7·6%).

The corresponding *acid*, obtained by hydrolysis with potassium hydrogen carbonate in aqueous methanol, separated from ethanol in yellow needles, m. p. 201—204° (Found: C, 56·0; H, 3·8; N, 7·7. $C_{25}H_{19}O_{11}N_3$ requires C, 55·9; H, 3·6; N, 7·8%).

Methyl 3 : 5-*Diacetamido*-4-(2 : 3-*dimethoxy*-5-2′-*phthalimidoethylphenoxy*)*benzoate*.—The dinitro-compound (0·175 g.) in acetic acid (5 c.c.) was hydrogenated at room temperature and atmospheric pressure with platinum. The catalyst was removed, 20% aqueous sodium

XUM

hydroxide (5 c.c.) and acetic anhydride (0·4 c.c.) were added, the mixture was shaken for 30 min., water added, and the solution was extracted with chloroform. Evaporation and crystallisation of the residue from ethanol gave the *diacetamido-derivative* in needles (0·141 g., 77%), m. p. 190—192° (Found: C, 62·3; H, 5·1. $C_{36}H_{29}O_9N_3$ requires C, 62·6; H, 5·2%).

Methyl 4-(2 : 3-*Dimethoxy*-5-2′-*phthalimidoethylphenoxy*)-3 : 5-*di-iodobenzoate* [IV; R = CH_2·CH_2·$N(CO)_2C_6H_4$-*o*, R′ = OMe].—(*a*) The dinitrobenzoate (2 g.) was reduced as described in the previous experiment, and the solution of the diamine was added during 1 hr. to a stirred solution of sodium nitrite (0·8 g.) in concentrated sulphuric acid (35 c.c.) and glacial acetic acid (25 c.c.). After 1 hr. the solution was added to a mixture of sodium iodide (3·5 g.), iodine (3 g.), urea (0·4 g.), water (200 c.c.), and chloroform (70 c.c.). The chloroform layer was separated, washed with aqueous sodium sulphite, and evaporated. The residue in acetone was chromatographed on acid-washed alumina. Elution with acetone gave a red oil. Further chromatography achieved no purification. The combined fractions with ethanol gave a red solid (1·6 g.), m. p. 135—175°. By treating a portion (1·1 g.) with a little acetone the *di-iodo-compound* was obtained as a white solid (0·80 g., 46%), separating from acetone–methanol in needles, m. p. 164—165°, and crystallising above this m. p. in prisms, m. p. 179—183° (Found: C, 44·5; H, 2·9; I, 35·6; OMe, 12·6. $C_{26}H_{21}O_7NI_2$ requires C, 43·8; H, 3·0; I, 35·6; 3OMe, 12·8%).

The crude mixture (0·5 g.) was triturated with ether. The precipitate (0·1 g., 14%) of 1-*iodo*-9 : 10-*dimethoxy*-3-*methoxycarbonyl*-7-2′-*phthalimidoethyldibenz*-1 : 4 : 5-*oxadiazepine*, crystallised from ethanol in orange prisms, m. p. 192—195° (Found: C, 50·8; H, 3·6; N, 6·9; I, 19·3. $C_{26}H_{20}O_7N_3I$ requires C, 50·9; H, 3·3; N, 6·9; I, 20·7%).

(*b*) In some experiments in which less of the di-iodo-compound was present, purification by chromatography was successful. Thus, the crude product from the dinitrobenzoate (1·12 g.) in acetone was chromatographed on a long column of acid-washed alumina. Elution with acetone and crystallisation from ethanol gave the di-iodo-compound in needles (0·21 g., 15%), m. p. 150—160°, resolidifying in prisms, m. p. 180—184°, undepressed by mixing with a sample obtained as in (*a*).

Further elution with acetone gave a red oil, affording from ethanol orange prisms (0·48 g., 39%), m. p. and mixed m. p. with the iodo-oxadiazepine 192—194°.

p-(2 : 3-*Dimethoxy*-5-2′-*phthalimidoethylphenoxy*)*benzoic Acid* [V; R = CH_2·CH_2·$N(CO)_2C_6H_4$-*o*, R′ = OMe].—Methyl 4-(2 : 3-dimethoxy-5-2′-phthalimidoethylphenoxy)-3 : 5-di-iodobenzoate, (0·6 g.) in ethyl acetate (50 c.c.) containing diethylamine (0·2 g.) was reduced with hydrogen and platinum at room temperature and atmospheric pressure until 2 mol. of hydrogen had been absorbed (30 min.). After filtration, the solution, which rapidly became red, was washed with dilute hydrochloric acid and water, and was evaporated. The residual red oil was extracted with several portions of boiling light petroleum (b. p. 60—80°), and the petroleum-soluble oil was refluxed for 2 hr. with potassium hydrogen carbonate in aqueous methanol. The gum, obtained by removal of the methanol, acidification, and extraction with chloroform, was heated at 140—150° for 30 min. Crystallisation from methanol and trituration of the solid with benzene furnished the *acid* in crystals (0·10 g., 27%), m. p. 180—183°, separating from benzene–light petroleum in prisms, m. p. 182—184°, and, after cooling and resolidifying, m. p. 197—202° (Found: C, 67·4; H, 4·5. $C_{15}H_{21}O_7N$ requires C, 67·1; H, 4·7%).

9 : 10-*Dimethoxy*-3-*methoxycarbonyl*-7-2′-*phthalimidoethyldibenz*-1 : 4 : 5-*oxadiazepine* (VI; R = H).—The iodo-oxadiazepine (0·30 g.) was hydrogenated as described for the di-iododiphenyl ether derivative, until hydrogen absorption ceased. The *product* crystallised from ethanol in yellow needles (0·23 g., 97%), m. p. 217—214° (Found: C, 64·3; H, 4·2; N, 8·2. $C_{26}H_{21}O_7N$ requires C, 64·3; H, 4·3; N, 8·6%).

Methyl 4-o-*Methoxyphenoxy*-3-*nitrobenzoate* (VIII; R = R′ = H).—A solution of methyl 3-chloro-4-nitrobenzoate (2·5 g.) and guaiacol (1·44 g.) in pyridine was heated under reflux for 1½ hr., added to ice and water, and extracted with ether. The ether solution was washed with dilute hydrochloric acid and dilute sodium hydroxide, then evaporated. By crystallisation from ethanol *methyl* 4-o-*methoxyphenoxy*-3-*nitrobenzoate* was obtained as plates (1·81 g., 51%), m. p. 97° (Found: C, 59·3; H, 4·4; N, 4·7. $C_{15}H_{13}O_6N$ requires C, 59·4; H, 4·3; N, 4·8%).

The *acid*, prepared by hydrolysis with potassium hydrogen carbonate, separated from ethyl acetate in prisms, m. p. 164° (Found: C, 58·2; H, 4·0. $C_{14}H_{11}O_6N$ requires C, 58·2; H, 3·8%).

4-*Methoxycarbonyl*-2-*nitrophenyl Toluene*-p-*sulphonate*.—Sodium carbonate (3 g.) was added in portions to a mixture of methyl 4-hydroxy-3-nitrobenzoate (3 g.), toluene-*p*-sulphonyl

chloride (3 g.), and water (30 c.c.) at 100°. After the addition of more toluene-*p*-sulphonyl chloride (0·5 g.) and sodium carbonate (0·5 g.), the solution was heated for a further 15 min. and cooled to 0°. The precipitate, after being washed with warm aqueous sodium carbonate and water, crystallised from ethanol, giving needles of the *toluene*-p-*sulphonate* (2·5 g., 50%), m. p. 95—96° (Found: C, 51·4; H, 3·7. $C_{15}H_{13}O_7NS$ requires C, 51·3; H, 3·8%).

iso*Vanillin Toluene*-p-*sulphonate*.—*iso*Vanillin (0·3 g.), toluene-*p*-sulphonyl chloride (0·6 g.), and diethylaniline (10 c.c.) were heated in a steam-bath for 2 hr. and added to dilute hydrochloric acid. The precipitated *ester* crystallised from ethanol as needles (0·5 g.), m. p. 144° (Found: C, 58·5; H, 4·7. $C_{15}H_{14}O_5S$ requires C, 58·8; H, 4·6%).

Methyl 4-(5-*Formyl*-2-*methoxyphenoxy*)-3-*nitrobenzoate* (VIII; R = CHO, R′ = H).—(*a*) A mixture of methyl 4-chloro-3-nitrobenzoate (0·5 g.), *iso*vanillin (0·5 g.), anhydrous potassium carbonate (1 g.), and ethyl methyl ketone (25 c.c.) was heated under reflux for 1·5 hr. After filtration and evaporation, the residue was washed in ether with aqueous sodium hydroxide and water. Evaporation of the ethereal layer and crystallisation of the residue from ethanol gave the *diphenyl ether* in needles (0·6 g., 60%), m. p. 118—121° (Found: C, 58·1; H, 4·1. $C_{16}H_{13}O_9N$ requires C, 58·0; H, 4·0%). The 2 : 4-*dinitrophenylhydrazone* separated from acetic acid in red prisms, m. p. 274° (Found: C, 51·9; H, 3·2. $C_{22}H_{17}O_{10}N_5$ requires C, 51·7; H, 3·4%).

(*b*) A solution of methyl 4-fluoro-3-nitrobenzoate (0·5 g.) and *iso*vanillin (0·5 g.) in pyridine (6·5 c.c.) was refluxed for 1½ hr., and added to dilute hydrochloric acid (50 c.c., 15%). Ether-extraction gave a brown oil (0·85 g.) which was chromatographed in benzene on alumina. Elution with light petroleum gave methyl 4-fluoro-3-nitrobenzoate (0·2 g.), and elution with benzene gave the diphenyl ether (0·6 g., 60%), m. p. and mixed m. p. 116—118°.

Reaction of 4-*Methoxycarbonyl*-2-*nitrophenyl Toluene*-p-*sulphonate with* iso*Vanillin*.—The toluene-*p*-sulphonate (1·0 g.), *iso*vanillin (0·5 g.), and potassium carbonate (1·5 g.) in dimethylformamide (30 c.c.) were heated under reflux for ½ hr. Addition of water and ether-extraction gave an oil which crystallised from ethanol in needles (0·9 g.), m. p. and mixed m. p. with *iso*vanillin toluene-*p*-sulphonate 140—142°.

Methyl 4-(5-*Formyl*-2 : 3-*dimethoxyphenoxy*)-3-*nitrobenzoate* (VIII; R = CHO, R′ = OMe).—(*a*) The potassium salt of 3-hydroxy-4 : 5-dimethoxybenzaldehyde [obtained from the aldehyde (4·9 g.) and potassium hydroxide in ethanol–ether as a brown oil] and methyl 4-chloro-3-nitrobenzoate (4·0 g.) were refluxed in diethylene glycol dimethyl ether (25 c.c.) for 1 hr. Water was added and the solution was extracted with ether. The ether was washed with aqueous sodium hydroxide and water and evaporated. The residue, on crystallisation from ethanol, afforded the *ether* (3·0 g., 31%), m. p. 88° (Found: C, 56·3; H, 4·0. $C_{17}H_{15}O_8N$ requires C, 56·5; H, 4·2%). Methyl 4-chloro-3-nitrobenzoate (2·5 g.), m. p. and mixed m. p. 74—76°, was recovered by concentration of the ethanol mother-liquor.

Acidification and ether-extraction of the alkaline washings gave 3-hydroxy-4 : 5-dimethoxybenzaldehyde (2·7 g., 55%), b. p. 125°/0·02 mm.

(*b*) 3-Hydroxy-4 : 5-dimethoxybenzaldehyde (0·5 g.) and methyl 4-chloro-3-nitrobenzoate (0·5 g.) were refluxed in pyridine (12 c.c.) for 1 hr., and the solution was added to dilute hydrochloric acid and extracted with ether. The ether solution was washed with aqueous sodium hydroxide and water and evaporated. The residue in light petroleum (b. p. 60—80°) was chromatographed on alumina. Elution with the same solvent gave methyl 4-chloro-3-nitrobenzoate (0·3 g.), m. p. and mixed m. p. 74—76°. Benzene elution gave the diphenyl ether (0·3 g., 35%), m. p. and mixed m. p. 80—84°. Further elution with benzene afforded a colourless by-product (0·25 g.), which did not crystallise.

The reaction was carried out under various conditions (Table 2).

Methyl 3-*Amino*-4-*o*-*methoxyphenoxybenzoate*.—Methyl 4-*o*-methoxyphenoxy-3-nitrobenzoate (0·73 g.) and 5% palladium–charcoal in ethyl acetate were hydrogenated at room temperature and atmospheric pressure. After filtration, the solution was evaporated. The residue, on trituration with light petroleum (b. p. 40—60°), gave the *amine*, separating from ethanol–light petroleum (b. p. 40—60°) in prisms (0·59 g., 90%), m. p. 70—71° (Found: C, 65·5; H, 5·5. $C_{15}H_{15}O_4N$ requires C, 65·5; H, 5·5%). The *acetyl derivative* crystallised from aqueous ethanol in needles, m. p. 121° (Found: C, 64·6; H, 5·2. $C_{17}H_{17}O_5N$ requires C, 64·8; H, 5·4%).

Methyl 4-(5-*Formyl*-2-*methoxyphenoxy*)*benzoate* (IX; R = CHO, R′ = H).—Methyl 4-(5-formyl-2-methoxyphenoxy)-3-nitrobenzoate (2 g.) in acetic anhydride (10 c.c.) was treated with concentrated sulphuric acid (4 drops). After 15 min., water was added, and the precipitated

gum washed with ethanol (2 × 10 c.c.). The *diacetate* crystallised from ethanol in needles, m. p. 109—111° (Found: C, 55·6; H, 4·3. $C_{20}H_{19}O_{10}N$ requires C, 55·4; H, 4·4%).

The crude product in ethyl acetate was hydrogenated with platinum at room temperature and atmospheric pressure. After filtration and evaporation the amine was treated in 15% hydrochloric acid (20 c.c.) at 0° during 20 min. with sodium nitrite (0·3 g.) in water. After 15 min. 30% hypophosphorous acid (30 c.c.) was added, the solution was kept at 0° for 12 hr., then extracted with ether, and the ether solution washed with dilute sodium hydroxide, dilute hydrochloric acid, and water. Evaporation and distillation of the residue gave the *aldehyde* (0·78 g., 45%), b. p. 200—220° (bath)/0·2 mm., separating from benzene–light petroleum (b. p. 40—60°) in prisms, m. p. 71—73° (Found: C, 67·5; H, 4·9. $C_{16}H_{14}O_5$ requires C, 67·1; H, 3·9%). The **2** : 4-*dinitrophenylhydrazone* crystallised from ethanol in red needles, m. p. 235° (Found: C, 56·5; H, 3·9. $C_{22}H_{18}O_8N_4$ requires C, 56·7; H, 3·9%).

Methyl 4-(5-*Formyl*-2 : 3-*dimethoxyphenoxy*)*benzoate* (IX; R = CHO, R′ = OMe).—Methyl 4-(5-formyl-2 : 3-dimethoxyphenoxy)-3-nitrobenzoate (3·2 g.) was acetylated, and the crude diacetate hydrogenated as in the preceding experiment. The amine in 15% hydrochloric acid (50 c.c.) at 0° was diazotised with sodium nitrite (0·5 g.) in water and, after 1 hr., 40% hypophosphorous acid (45 c.c.) and copper sulphate (10 mg.) were added. The solution was kept at 0° for 4 hr. and extracted with ether. After being washed with alkali and acid the ether solution was evaporated, and the residue (2·2 g.) in benzene chromatographed on alumina. *Methyl* 4-(5-*formyl*-2 : 3-*dimethoxyphenoxy*)*benzoate* was obtained by benzene elution, and separated from light petroleum (b. p. 40—60°) in needles (2·0 g., 70%), m. p. 111—113° (Found: C, 64·4; H, 5·1. $C_{17}H_{16}O_6$ requires C, 64·6; H, 5·1%).

4-(5-*Formyl*-2 : 3-*dimethoxyphenoxy*)*benzoic Acid* (X).—A solution of the ester (2·8 g.) and potassium hydrogen carbonate (15 g.) in methanol (100 c.c.) and water (40 c.c.) was heated under reflux for 2 hr. The methanol was removed, and the solution was acidified with dilute hydrochloric acid. The precipitated *acid* crystallised from benzene–light petroleum (b. p. 60—80°) in plates (2·1 g., 80%), m. p. 73—74°, and after being heated at 25°/0·001 mm. for 3 hr., 118—120° (Found: C, 63·4; H, 4·6. $C_{16}H_{14}O_6$ requires C, 63·6; H, 4·7%).

4-(2 : 3-*Dimethoxy*-5-2′-*nitrovinylphenoxy*)*benzoic Acid* (XI).—5% Aqueous sodium hydroxide (3·5 c.c.) was added during 20 min. to a solution of 4-(5-formyl-2 : 3-dimethoxyphenoxy)benzoic acid (0·35 g.) at 0—10°. After 20 min., the solution was added to 15% hydrochloric acid (30 c.c.) Crystallisation of the precipitate from aqueous ethanol gave the *nitrovinyl-acid* as yellow needles (0·25 g., 63%), m. p. 164—167° (Found: C, 59·3; H, 4·7. $C_{17}H_{15}O_7N$ requires C, 59·1; H, 4·4%).

p-(2 : 3-*Dimethoxy*-5-2′-*phthalimidoethylphenoxy*)*benzoic Acid* [V; R = $CH_2{\cdot}CH_2{\cdot}N(CO)_2C_6H_4$-*o*, R′ = OMe].—The nitrovinyl-derivative (0·40 g.), acetic acid (35 c.c.), concentrated sulphuric acid (0·3 c.c.), and platinum oxide (200 mg.) were hydrogenated at room temperature and atmospheric pressure until hydrogen absorption ceased (1 hr.). After filtration, the solution was evaporated, and the residue in water passed through a column of ion-exchange resin (Amberlite IR-4B). The eluate, on evaporation, afforded p-(5-2′-*aminoethyl*-2 : 3-*dimethoxyphenoxy*)*benzoic acid* (0·35 g.), which, sublimed at 225—230° (bath)/0·0001 mm., had m. p. 260—264° (Found: C, 64·2; H, 6·0. $C_{17}H_{19}O_5N$ requires C, 64·3; H, 6·0%).

The crude amino-acid was heated at 140—160° for 2 hr. with phthalic anhydride (0·18 g.). The melt was extracted with chloroform, and the residue heated with a further quantity of phthalic anhydride and extracted with chloroform. Evaporation of the chloroform solution and crystallisation of the residue from methanol gave the phthalimido-acid (0·22 g., 43%), m. p. 180—190°. Recrystallisation from methanol gave cubes, m. p. 197—202°, identical (mixed m. p. and infrared spectrum) with a sample prepared by the alternative route.

The authors thank Parke, Davis and Co. Ltd. for a Research Fellowship (to J. R. L.), the Colonial Products Council for a Studentship (to J. R. C.), and Dr. J. D. Loudon for helpful discussion.

University of Glasgow,
The Queen's University of Belfast.

[*Received, January 10th*, 1958.]

439. *The Preparation and Donor Properties of Some Silylamines.*

By E. A. V. Ebsworth and H. J. Emeléus.

Tri(methylsilyl)amine, $(Me{\cdot}SiH_2)_3N$, *N*-methyldi(methylsilyl)amine, $Me{\cdot}N(SiH_2Me)_2$, and *NN*-dimethyl(methylsilyl)amine, $Me_2N{\cdot}SiH_2Me$, have been prepared and characterised. Physical properties of *NN*-dimethyl(trimethylsilyl)amine, $Me_2N{\cdot}SiMe_3$, have been determined. The electron-donor properties of the nitrogen atoms in these compounds towards trimethylboron, methyl iodide, methyliodosilane, hydrogen halides, and boron trifluoride have been studied; in some cases relatively stable adducts were formed. Equimolar addition compounds of trimethylamine with methyl-fluoro-, -chloro-, -bromo-, and -iodo-silane have been prepared.

Trisilylamine, $(SiH_3)_3N$, was first prepared by Stock and Somieski [1] by the reaction of excess of silyl chloride with ammonia in the vapour phase. With excess of ammonia the main product was disilylamine, $(SiH_3)_2NH$; this decomposed at room temperature giving silane, trisilylamine, and solid polymers. *N*-Methyldisilylamine was made similarly from methylamine and silyl chloride; [2] *NN*-dimethylsilylamine, however, could not be isolated from the products of the reaction of silyl chloride and dimethylamine,[2] and was eventually made from silyl bromide and dimethylamine.[3] Triorganosubstituted halogenosilanes also react with amines containing hydrogen bound to nitrogen to give silylamines,[4] but the product depends on the size of the organic groups.[5] In this way a few *Si*-trimethylsilylamines have been made from trimethylchlorosilane,[6] but no attempt has been made to study systematically the effect of methyl-substitution in the silyl group on the donor properties of the nitrogen atom. This was the purpose of preparing the three new amines described below.

Tri(methylsilyl)amine was prepared from ammonia and excess of methylchlorosilane. The products included an unstable material, believed to be di(methylsilyl)amine, $(Me{\cdot}SiH_2)_2NH$; a similar substance was formed when an excess of ammonia was used. *N*-Methyldi(methylsilyl)amine, $Me{\cdot}N(SiH_2Me)_2$, was prepared similarly from methylamine and methylchlorosilane:

$$2Me{\cdot}SiH_2Cl + 3Me{\cdot}NH_2 = Me{\cdot}N(SiH_2Me)_2 + 2Me{\cdot}NH_3Cl$$

In view of the difficulty of isolating *NN*-dimethylsilylamine,[2] *NN*-dimethyl(methylsilyl)amine was made from dimethylamine and methyliodosilane rather than from methylchlorosilane; the products included the addition compound of the amine and methyliodosilane, which was later prepared from its two components. *NN*-Dimethyl(trimethylsilyl)amine was made as described by Mjörne.[7]

Tri(methylsilyl)amine was decomposed at −78° by dry hydrogen chloride, giving ammonium chloride and methylchlorosilane:

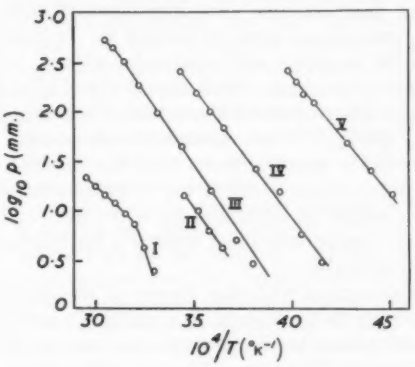
$$(Me{\cdot}SiH_2)_3N + 4HCl = 3Me{\cdot}SiH_2Cl + NH_4Cl$$

The three other amines reacted similarly, and this behaviour is like that of most other silylamines.[1,2,3] Only two compounds containing silicon bound to nitrogen are known to form adducts with a hydrogen halide; [8] they are *NN*-dimethyl(trichlorosilyl)amine,

[1] Stock and Somieski, *Ber.*, 1921, **54**, 740.
[2] Emeléus and Miller, *J.*, 1939, 819.
[3] Sujishi and Witz, *J. Amer. Chem. Soc.*, 1954, **76**, 4631.
[4] Kraus and Rosen, *ibid.*, 1925, **47**, 2739; Larsson and Mjörne, *Trans. Chalmers Univ. Göttenburg*, 1949, No. 87, 29; Bailey, Sommer, and Whitmore, *J. Amer. Chem. Soc.*, 1948, **70**, 435.
[5] Brewer and Haber, *ibid.*, 1948, **70**, 3888.
[6] Sauer and Hasek, *ibid.*, 1946, **68**, 241.
[7] Mjörne, *Svensk kem. Tidskr.*, 1950, **62**, 120.
[8] Cass and Coates, *J.*, 1952, 2347.

$Me_2N{\cdot}SiCl_3$, and tetra-*N*-methyl(dichlorosilylylene)diamine, $(Me_2N)_2SiCl_2$. The structures of the adducts are not known.

One of the reasons why silylamines can be prepared from halogenosilanes and ammonia or amines is that they do not as a rule form quaternary compounds,[1,2] although halogenosilanes give adducts with tertiary aliphatic amines.[2,9,10] Tri(methylsilyl)amine and *N*-methyldi(methylsilyl)amine were found to conform to this pattern; when methyl iodide was mixed with either, it was recovered unchanged.[11] Methyl iodide reacted with both *NN*-dimethyl(methylsilyl)amine and *NN*-dimethyl(trimethylsilyl)amine, however, forming stable, solid 1 : 1 adducts. The last amine formed no adduct with methyl chloride. Similarly, methyliodosilane did not react with tri(methylsilyl)amine or *N*-methyldi(methylsilyl)amine; with *NN*-dimethyl(methylsilyl)amine it reacted violently at low temperatures to form a 1 : 1 adduct whose vapour density showed it to be completely dissociated in the vapour phase. The dissociation products were identified spectroscopically as methyliodosilane and the original amine. The dissociation was initially reversible at 0°, but the compound decomposed slowly at room temperature, probably because of disproportionation of the halide. Dissociation-pressure measurements (5—45°) gave an approximately



Dissociation pressures of addition compounds of methylhalogenosilanes.
I, Trimethylamine–methyliodosilane.
II, Trimethylamine–methylbromosilane.
III, NN-Dimethyl(methylsilyl)amine–methyliodosilane.
IV, Trimethylamine–methylchlorosilane.
V, Trimethylamine–methylfluorosilane.

linear plot of $\log_{10} p$ against $1/T$, leading to a heat of dissociation of *ca.* 10 kcal. mole^{-1}. *NN*-Dimethyl(trimethylsilyl)amine also reacted with methyliodosilane, giving a solid equimolar adduct; this however gave complex products when vaporized. In view of the formation of definite adducts by *NN*-dimethylsilylamines, the behaviour of trimethylamine itself was examined. In this case equimolar compounds were formed with all of the four methylhalogenosilanes $Me{\cdot}SiH_2X$ (X = F, Cl, Br, or I). Dissociation-pressure measurements for the series are shown in the Figure as plots of $\log_{10} p$ against $1/T$; the fluoride and the bromide adduct were shown spectroscopically to dissociate to their original components in the vapour phase, and dissociation was shown by vapour-density measurements to be virtually complete.

Although the graphs for the fluoride and the chloride compound are almost linear, the dissociation pressures were not exactly reproducible with descending temperature. This is probably due to the rapid disproportionation of the methylhalogenosilanes.[10] The results do, nevertheless, establish the order of stability of the adducts. They also lead to heats of dissociation of the order of 10 kcal. mole^{-1}.

With trimethylboron neither tri(methylsilyl)amine nor *N*-methyldi(methylsilyl)amine gave an adduct, and recovery of the boron compound was quantitative. With *NN*-dimethyl(methylsilyl)amine and *NN*-dimethyl(trimethylsilyl)amine, reaction occurred in

[9] Aylett, Emeléus, and Maddock, *J. Inorg. Nuclear Chem.*, 1955, **1**, 187.
[10] Miller, Ph.D. Thesis, London, 1939.
[11] For details of this and other negative experiments see Ebsworth, Ph.D. Thesis, Cambridge, 1957.

approximately equimolar ratios; the solid products melted at *ca.* −35° and −40° to −30° respectively.

The experiments on the formation of compounds between the silylamines and either boron trifluoride or trichloride showed that the adducts initially formed were unstable. Thus, with boron trifluoride, tri(methylsilyl)amine reacted at −78°, to give a crystalline solid; this decomposed rapidly in the presence of excess of boron trifluoride to give methylfluorosilane and *NN*-di(methylsilyl)aminoboron difluoride:

$$(Me{\cdot}SiH_2)_3N + BF_3 = (Me{\cdot}SiH_2)_3N,BF_3$$
$$(Me{\cdot}SiH_2)_3N,BF_3 = Me{\cdot}SiH_2F + (Me{\cdot}SiH_2)_2N{\cdot}BF_2$$

NN-Dimethyl(methylsilyl)amine similarly gave methylsilyl fluoride and *NN*-dimethylaminoboron difluoride, while *NN*-dimethyl(trimethylsilyl)amine gave trimethylfluorosilane and *NN*-dimethylaminoboron difluoride:

$$Me_3Si{\cdot}NMe_2 + BF_3 = Me_3Si{\cdot}NMe_2,BF_3$$
$$Me_3Si{\cdot}NMe_2,BF_3 = Me_3SiF + Me_2N{\cdot}BF_2$$

These reactions are very like those recently described between silylamines containing SiH_3 groups and boron trifluoride.[12] Tri(methylsilyl)amine reacted with boron trichloride at −78° to give a solid equimolar adduct, but this decomposed when warmed, forming a variety of products which included methylchlorosilane.

The above results show that the methylated silylamines, like those containing the SiH_3 group,[1,13] are comparatively weak bases. The *NN*-dimethylsilylamines are appreciably stronger bases than the others,[3] but no acceptor has yet been found which will differentiate between the *N*-methyldisilylamines and the trisilylamines. These form only unstable adducts, and any attempt to assess relative base-strengths from the stabilities of such compounds must assume a knowledge of the mechanisms of decomposition which is not available.

This agrees with the theory of $d\pi$-bonding between silicon and amino-nitrogen.[14,15] According to the theory, the nitrogen's lone pair of electrons can pass partly into vacant 3*d* orbitals on the silicon atom, and thus becomes less readily available to external electron-acceptors. This cannot happen with carbon, which has no 3*d* orbitals in its outer shell; hence each successive substitution of silicon for carbon in the methylamines should lead to a drop in the basic properties of the resulting amine.

It is less easy to see how silicon-methylation affects the donor properties of the nitrogen atom. It is only possible to compare the base-strengths of the three *NN*-dimethylsilylamines, for only these form reasonably stable addition compounds. Towards trimethylboron, the dissociation pressures of the adducts suggest that silicon-methylation weakens the B–N bond; this would be expected for steric reasons, and is probably not an electronic effect. The other differences between the three amines can be put down to steric influences, and there is no evidence to suggest that silicon-methylation has any marked effect on the nitrogen atom's electron-donor properties.

Experimental

Preparation of Methylchlorosilane and Methylbromosilane.—Methyliodosilane (1 g.) was passed as vapour through a tube packed with dried powdered mercuric chloride (30 g.). Methylchlorosilane was isolated by fractionation, in 90% yield based on the equation $2Me{\cdot}SiH_2I + HgCl_2 = 2Me{\cdot}SiH_2Cl + HgI_2$ (Found: *M*, 81·5; v. p. 63 mm. at −45°; m. p. −135°. Calc. for CH_5ClSi: *M*, 80·5; v. p. 63 mm. at −45°; m. p. −135°).

[12] Sujishi and Witz, *J. Amer. Chem. Soc.*, 1957, **79**, 2447.
[13] Burg and Kuljian, *ibid.*, 1950, **72**, 3103.
[14] Craig, Maccoll, Nyholm, Orgel, and Sutton, *J.*, 1954, 332.
[15] Hedburg, *J. Amer. Chem. Soc.*, 1955, **77**, 6491.

Methyliodosilane (1·5 g.) was passed as vapour over dried powdered silver bromide (40 g.) mixed with glass wool (40 g.). From the volatile products *methylbromosilane* was isolated by fractional distillation at −96° (Found: *Si*-H, 1·60; Br, 63·0%; *M*, 126. CH_5BrSi requires *Si*-H, 1·60; Br, 63·6%; *M*, 125). The m. p. was −119°. The v. p. was given in the range −10° to 23° by $\log_{10} p$ (mm.) = 7·732 − 1490/*T*. The extrapolated b. p. was 34° ± 0·5°, the latent heat of vaporization 6800 cal./mole, and Trouton's constant 21·8. The infrared spectrum is described elsewhere.[16] The yield was 93% based on the equation $Me{\cdot}SiH_2I + AgBr = Me{\cdot}SiH_2Br + AgI$.

Preparation of Tri(methylsilyl)amine.—In a typical experiment methylchlorosilane (0·593 g.) was mixed with ammonia (0·163 g.) in the vapour phase at room temperature. The pressures of the reactants were controlled so as to keep an excess of halide in the reaction-vessel. *Tri(methylsilyl)amine* was isolated by fractional distillation and condensation of the products (Found: C, 24·2; H, total, 10·2; *Si*-H, 4·0; N, 9·5%; *M*, 149. $C_3H_{15}NSi_3$ requires C, 24·0; H, total, 10·0; *Si*-H, 4·04; N, 9·4%; *M*, 149). The m. p. was −107°. The v. p. was given in the range 50—105° by $\log_{10} p$ (mm.) = 7·491 − 1760/*T*. The extrapolated b. p. was 108·6° ± 0·2°, the latent heat of vaporization 8100 cal./mole, and Trouton's constant 20·7. The compound absorbed in the ultraviolet region below 2500 Å, and there was no maximum above 2000 Å. The infrared spectrum is described elsewhere.[16] The yield was 65—70% based on the equation $3Me{\cdot}SiH_2Cl + 4NH_3 = (Me{\cdot}SiH_2)_3N + 3NH_4Cl$. A second product which decomposed slowly at room temperature to tri(methylsilyl)amine and other products was tentatively identified as *di(methylsilyl)amine* (Found: *M*, 112. $C_2H_{11}NSi_2$ requires *M*, 105).

Reaction of Tri(methylsilyl)amine with Hydrogen Chloride.—Hydrogen chloride (0·096 g.) and tri(methylsilyl)amine (0·059 g.), when mixed at −78°, formed a white solid. After 18 hr. hydrogen chloride (0·040 g.) was recovered (Found: *M*, 35·5; v. p. 10 mm. at −136°. Calc. for HCl: *M*, 36·5; v. p. 10 mm. at −136°), with methylchlorosilane (0·094 g.) (Found: *M*, 81; v. p. 51·9 mm. at −46°. Calc. for CH_5ClSi: *M*, 80·5; v. p. 56 mm. at −46°). The chloride in the residue corresponded with 0·020 g. of ammonium chloride.

Reaction of Tri(methylsilyl)amine with Boron Trichloride.—An equimolar mixture of boron trichloride (0·058 g.) and tri(methylsilyl)amine (0·074 g.) was solid at −78°, the m. p.s of both components being the same, −107°. The solid melted with gas evolution at −46° and did not freeze on re-cooling to −78°. The volatile products isolated were: hydrogen chloride (0·007 g.); an inseparable mixture of boron trichloride and methylchlorosilane (0·030 g.), shown to contain 0·023 g. of the latter by measurement of the hydrogen evolved on alkaline hydrolysis; and a heavy, barely volatile liquid which decomposed slowly at room temperature leaving a white involatile solid residue. When an initial excess of amine was taken, pure methylchlorosilane was recovered in place of the mixture with boron trichloride.

Reaction of Tri(methylsilyl)amine with Boron Trifluoride.—An equimolar mixture of boron trifluoride (0·048 g.) and tri(methylsilyl)amine (0·104 g.) solidified at −78°. The volatile products were a mixture of boron trifluoride and methylfluorosilane (0·044 g.), with a less volatile material which was probably a mixture of tri(methylsilyl)amine and *NN*-di(methylsilyl)aminoboron difluoride (see below).

A mixture of boron trifluoride (0·132 g.) and tri(methylsilyl)amine (0·146 g.) was liquid at −96°. After 18 hr. at −78° the products volatile at −96° were boron trifluoride (0·064 g.) (Found: *M*, 67·5; v. p. 31 mm. at −133°. Calc. for BF_3: *M*, 67·8; v. p. 34 mm. at −133°) and methylfluorosilane (0·059 g.) (Found: *M*, 65; v. p. 27·2 mm. at −96°, 100 mm. at −78°. Calc. for CH_5FSi: *M*, 64; v. p. 28 mm. at −96°, 104 mm. at −78°). The residue, involatile at −96°, was *NN-di(methylsilyl)aminoboron difluoride* (Found: *Si*-H, 2·52; B, ~7·3%; *M*, 152. $C_2H_{10}F_2NBSi_2$ requires *Si*-H, 2·61; B, 6·65%; *M*, 152). The compound was stable in glass at room temperature, but decomposed rapidly in the presence of tap-grease. The yield of methylfluorosilane was 95%, and of *NN*-di(methylsilyl)aminoboron difluoride 80%, based on the equation $(Me{\cdot}SiH_2)_3N + BF_3 = (Me{\cdot}SiH_2)_2N{\cdot}BF_2 + Me{\cdot}SiH_2F$; each mole of amine combined with 1·02 moles of boron trifluoride.

Preparation of N-*Methyldi(methylsilyl)amine.*—Methylamine (0·370 g.) and methylchlorosilane (0·790 g.) were mixed in the vapour phase, the halide being kept as far as possible in excess. From the volatile products N-*methyldi(methylsilyl)amine* (0·300 g.) was isolated by fractional distillation at −64° and condensation at −96°. It was purified by condensation at −78° (Found: *Si*-H, 3·36; N, 12·0%; *M*, 119. $C_3H_{13}NSi_2$ requires *Si*-H, 3·38; N, 11·8%;

[16] Ebsworth, Onyszchuk, and Sheppard, *J.*, 1958, 1453.

M, 119). The m. p. was −115°. The v. p. at 0° was 27·5 mm., and between 30° and 78° was expressed by $\log_{10} p$ (mm.) = 7·646 − 1683/*T*. The extrapolated b. p. was 80·1° ± 0·2°, the latent heat of vaporization 7700 cal./mole, and Trouton's constant 21·7. The yield was 65% based on the equation $2Me{\cdot}SiH_2Cl + 3Me{\cdot}NH_2 = Me{\cdot}N(SiH_2Me)_2 + 2Me{\cdot}NH_2Cl$.

Reaction of N-*Methyldi*(*methylsilyl*)*amine with Hydrogen Chloride*.—Hydrogen chloride (0·101 g.) and *N*-methyldi(methylsilyl)amine (0·065 g.) when mixed at 78° formed a white solid. After 18 hr. hydrogen chloride (0·039 g.) was recovered (Found: *M*, 35; v. p. 373 mm. at −96°. Calc. for HCl: *M*, 36·5; v. p. 390 mm. at −96°), with methylchlorosilane (0·089 g.) (Found: *M*, 82; v. p. 51 mm. at −47°. Calc. for CH_5ClSi: *M*, 80·5; v. p. 52 mm. at −47°). The chloride in the solid residue corresponded with 0·038 g. of methylamine hydrochloride.

Preparation of NN-*Dimethyl*(*methylsilyl*)*amine*.—Dimethylamine (0·345 g.) and methyliodosilane (0·730 g.) were mixed in the vapour phase at room temperature, the amine being kept as far as possible in excess. From the products, NN-*dimethyl*(*methylsilyl*)*amine* (0·310 g.) was isolated by fractionation (Found: *Si*-H, 2·26; N, 15·3%; *M*, 89. $C_3H_{11}NSi$ requires *Si*-H, 2·24; N, 15·7%; *M*, 89). The compound solidified to a clear glass which softened at −150° to −160°. The v. p. at 0° was 127 mm. and in the range 0—44° was given by $\log_{10} p$ (mm.) = 7·505 − 1474/*T*. The extrapolated b. p. was 45·3° ± 0·2°, the latent heat of vaporization 6750 cal./mole, and Trouton's constant 21·3. The yield was 90% based on the equation $Me{\cdot}SiH_2I + 2Me_2NH = Me_2N{\cdot}SiH_2Me + Me_2NH_2I$. An unstable volatile white solid was also formed in the reaction: it was involatile at −64°, and was identified as the adduct $Me_2N{\cdot}SiH_2Me,Me{\cdot}SiH_2I$, described below.

Reaction of NN-*Dimethyl*(*methylsilyl*)*amine with Hydrogen Chloride*.—Hydrogen chloride (0·089 g.) and *NN*-dimethyl(methylsilyl)amine (0·073 g.) formed a white solid at −78°. After 18 hr. hydrogen chloride (0·035 g.) was recovered (Found: *M*, 38; v. p. 13 mm. at −134°. Calc. for HCl: *M*, 36·5; v. p. 13 mm. at −134°), with methylchlorosilane (0·065 g.) (Found: *M*, 80; v. p. 61 mm. at −46°. Calc. for CH_5ClSi: *M*, 80·5; v. p. 56 mm. at −46°). The chloride in the solid residue corresponded with 0·065 g. of dimethylamine hydrochloride.

Reaction of N-*Dimethyl*(*methylsilyl*)*amine with Trimethylboron*.—An equimolar mixture of *NN*-dimethyl(methylsilyl)amine (0·052 g.) and trimethylboron (0·031 g.) was solid at −64°; the m. p.s of the components are −100° and ~−150° and neither component could be recovered at −96°, showing that neither was in excess. The vapour density at 20° of a completely vaporized sample gave *M*, 73 (a completely dissociated adduct requires *M*, 72). The dissociation pressures, measured with a dead space of ~50 ml., were:

p (mm.)	6·5	11·0	15·5	20·5	26·5	43·0	180
Temp.	−64°	−46°	−39°	−35°	−30°	−23°	0°

The solid melted at ~−35°.

Reaction of NN-*Dimethyl*(*methylsilyl*)*amine with Methyl Iodide*.—Methyl iodide (0·158 g.) and *NN*-dimethyl(methylsilyl)amine (0·039 g.) were mixed at room temp. White crystals were formed gradually, and the material appeared solid after 3 days. Methyl iodide (0·089 g.) was recovered (Found: *M*, 135; v. p. 142 mm. at 0°. Calc. for CH_3I: *M*, 142; v. p. 141 mm. at 0°). This methyl iodide could not be fully purified from what was probably a decomposition product of the amine. If the methyl iodide recovered is assumed to be pure, the molar combining ratio was 0·91 : 1. The *solid* was involatile in a vacuum (Found: I, 54·5. $C_4H_{14}NISi$ requires I, 55·0%).

Reaction of NN-*Dimethyl*(*methylsilyl*)*amine with Methyliodosilane*.—*NN*-Dimethyl(methylsilyl)amine (0·028 g.) and methyliodosilane (0·389 g.) reacted vigorously at −50°, forming a white solid. Excess of methyliodosilane (0·333 g.) was recovered (Found: *M*, 167; v. p. 49·0 mm. at 1°. Calc. for CH_5ISi: *M*, 172; v. p. 46·0 mm. at 1°). The molar reacting ratio was 0·97 : 1. The solid was involatile at −46° (Found: *Si*-H, 1·48; I, 48·9%. $C_4H_{16}Si_2N$ requires *Si*-H, 1·53; I, 48·7%). The dissociation was initially reversible, the infrared spectrum of the vapour being identical with that expected of a mixture of the two reactants. The vapour density showed the dissociation to be virtually complete (Found: *M*, 127, 135. A completely dissociated *adduct* requires *M*, 130). Slow decomposition occurred at room temperature and a liquid was formed. Methylsilane (0·023 g.) was recovered after three weeks (Found: *M*, 44; 76 mm. at −96°. Calc. for CH_6Si: *M*, 46; v. p. 84 mm. at −86°).

Reaction of NN-*Dimethyl*(*methylsilyl*)*amine with Boron Trifluoride*.—An equimolar mixture of *NN*-dimethyl(methylsilyl)amine (0·075 g.) and boron trifluoride (0·057 g.) was solid at −78°.

The solid melted below room temperature and, after warming to about 60°, methylfluorosilane (0·040 g.) was recovered (Found: *M*, 64; v. p. 98 mm. at −78°. Calc. for CH_5FSi: *M*, 64; v. p. 104 mm. at −78°). A crystalline residue remained, which was shown spectroscopically to be *NN*-dimethylaminoboron difluoride.

Preparation of NN-*Dimethyl*(*trimethylsilyl*)*amine*.—Mjörne's method [7] was used. The product was purified by fractional distillation at −64° (Found: C, 50·3; H, 12·7; N, 11·8%; *M*, 117. Calc. for $C_5H_{15}NSi$: C, 51·2; H, 12·8; N, 11·9%; *M*, 117). The v. p. was 22·5 mm. at 0°, and in the range 40—84° was given by $\log_{10} p$ (mm.) = 7·491 − 1657/*T*. The b. p. was 86·2° ± 0·2°, the latent heat of vaporization 7600 cal./mole, and Trouton's constant 21·1.

Reaction of NN-*Dimethyl*(*trimethylsilyl*)*amine with Hydrogen Chloride*.—*NN*-Dimethyl(trimethylsilyl)amine (0·063 g.) and hydrogen chloride (0·074 g.) gave a white solid at −78°. After 18 hr., hydrogen chloride (0·035 g.) was recovered (Found: *M*, 37; v. p. 82·5 mm. at −117°. Calc. for HCl: *M*, 36·5; v. p. 80 mm. at 117°), with trimethylchlorosilane (0·052 g.) (Found: *M*, 109; v. p. 72 mm. at 0°. Calc. for C_3H_9ClSi: *M*, 109; v. p. 74 mm. at 0°). The solid residue contained chloride corresponding with 0·065 g. of dimethylamine hydrochloride.

Reaction of NN-*Dimethyl*(*trimethylsilyl*)*amine with Hydrogen Iodide*.—*NN*-Dimethyl(trimethylsilyl)amine (0·074 g.) and hydrogen iodide (0·228 g.) formed a solid at −78°, which decomposed at room temperature. Hydrogen iodide (0·063 g.) was recovered (Found: *M*, 126; v. p. 154 mm. at −65°. Calc. for HI: *M*, 128; v. p. 162 mm. at −65°) and trimethyliodosilane (0·100 g.) (Found: I, 60·5%; *M*, 200. Calc. for C_3H_9ISi: I, 63·5%; *M*, 200).

Reaction of NN-*Dimethyl*(*trimethylsilyl*)*amine with Trimethylboron*.—*NN*-Dimethyl(trimethylsilyl)amine (0·092 g.) and trimethylboron (0·106 g.) gave a product which was solid at −64°. Trimethylboron (0·063 g.) was recovered by distillation at −96° (Found: *M*, 56; v. p. 30 mm. at −79°. Calc. for C_3H_9B: *M*, 56; v. p. 31 mm. at −79°). The combining ratio was 1·02 : 1. A sample when completely vaporized at 20° had *M* 84 (a completely dissociated *adduct* requires *M* 86·5). The dissociation pressures, measured in a dead space of 50 ml., were:

p (mm.)	6·0	11·3	40·4	108·0	141·5	183·5	218
Temp.	−64°	−45°	−34°	−23°	−18°	−11°	0°

Reaction of NN-*Dimethyl*(*trimethylsilyl*)*amine with Methyl Iodide*.—The amine (0·101 g.) and methyl iodide (0·258 g.) reacted slowly at room temperature, forming white crystals. After 3 days the residual volatile material was methyl iodide (0·136 g.) (Found: *M*, 139; v. p. 139 mm. at 0°. Calc. for CH_3I: *M*, 142, v. p. 141 mm. at 0°). The molar combining ratio was 1·01 : 1. The white *solid* was involatile in a vacuum at room temperature (Found: I, 49·7. $C_6H_{16}NISi$ requires I, 49·0%). The solid was unchanged after 18 hr. at 110°.

Reaction of NN-*Dimethyl*(*trimethylsilyl*)*amine with Methyliodosilane*.—The amine (0·035 g.) and methyliodosilane (0·224 g.) reacted at −46°, to form a white solid. Methyliodosilane (0·174 g.) was recovered (Found: *M*, 174; v. p. 43 mm. at 0°. Calc. for CH_5ISi: *M*, 172; v. p. 43 mm. at 0°). The molar reacting ratio was 1·00 : 1. The solid had a v. p. of ~10 mm. at 20°, but decomposition occurred on sublimation at room temperature and a white involatile solid residue remained.

Reaction of NN-*Dimethyl*(*trimethylsilyl*)*amine with Boron Trifluoride*.—The amine (0·053 g.) and boron trifluoride (0·140 g.) formed a white solid at room temperature. Boron trifluoride (0·109 g.) was recovered (Found: *M*, 68; v. p. 191 mm. at −118°. Calc. for BF_3: *M*, 67·8; v. p. 173 mm. at −118°). The solid was involatile at room temperature; it vaporized at 100°, producing trimethylfluorosilane (0·035 g.) (Found: *M*, 93; v. p. 125 mm. at −23°. Calc. for C_3H_9FSi: *M*, 92; v. p. 124 mm. at −23°), while crystals of *NN*-dimethylaminoboron difluoride were deposited (Found: C, 25·8; H, 6·7. Calc. for $C_2H_6NF_2B$: C, 25·9; H, 6·7%). The infrared spectrum of the crystals was identical with that of the sample prepared from *NN*-dimethyl(methylsilyl)amine (see above). For each mole of amine taken, 0·99 mole of boron trifluoride was consumed and 0·82 mole of trimethylfluorosilane was produced.

Reactions of Trimethylamine.—(a) *With methylfluorosilane*. Trimethylamine (0·188 g.) and methylfluorosilane (0·326 g.) gave a solid product at −96°; methylfluorosilane (0·214 g.) was recovered (Found: *M*, 65; v. p. 106 mm. at −78°. Calc. for CH_5FSi: *M*, 64; v. p. 100 mm. at −78°). The molar combining ratio was 0·96 : 1. The solid was volatile at −64°, and dissociated reversibly up to −46°. The extrapolated dissociation pressure was 1 atm. at −16°. The vapour density showed the compound to be completely dissociated in the vapour

phase (Found: *M*, 62. A completely dissociated *adduct* requires *M*, 62·5); the dissociation products were identified spectroscopically as trimethylamine and methylfluorosilane.

(b) *With methylchlorosilane.* Trimethylamine (0·032 g.) and methylchlorosilane (0·065 g.) formed a white *solid* at −46° (Found: *Si*-H, 1·35; Cl, 25·3. $C_4H_{14}NClSi$ requires *Si*-H, 1·43; Cl, 25·4%); methylchlorosilane (0·021 g.) was recovered (Found: *M*, 78; v. p. 60 mm. at −45°. Calc. for CH_5ClSi: *M*, 80·5; v. p. 63 mm. at −45°). The molar combining ratio was 1·00 : 1. Dissociation pressures of the solid were measured: there was some decomposition above 0°. The vapour had *M* 70 (a completely dissociated adduct requires *M* 70·5).

(c) *With methylbromosilane.* Trimethylamine (0·053 g.) and methylbromosilane (0·261 g.) formed a white *solid* at 0° (Found: *Si*-H, 1·08; Br, 43·0. $C_4H_{14}NBrSi$ requires *Si*-H, 1·09; Br, 43·4%); methylbromosilane (0·154 g.) was recovered at −46° (Found: *M*, 125; v. p. 191 mm. at 0°. Calc. for CH_5BrSi: *M*, 125; v. p. 196 mm. at 0°). The molar combining ratio was 1·04 : 1. The solid had a dissociation pressure of 4 mm. at 0°; dissociation was not reversible between 0° and 10°; the dissociation products were identified spectroscopically as the original reactants.

(d) *With methyliodosilane.* Trimethylamine (0·026 g.) and methyliodosilane (0·167 g.) reacted vigorously together at −50°, forming white crystals. Methyliodosilane (0·092 g.) was recovered (Found: *M*, 169; v. p. 46 mm. at 1°. Calc. for CH_5ISi: *M*, 172; v. p. 46 mm. at 1°). Vapour pressures were recorded up to 110°, but the graph of log *p* against $1/T$ was not linear, nor was the dissociation reversible. The dissociation pressure at 20° was *ca.* 1 mm.

The authors are grateful to Dr. A. G. Maddock for the interest he has shown in this work. One of them (E. A. V. E.) thanks King's College, Cambridge, for a Harold Fry Studentship, and the Department of Scientific and Industrial Research for a maintenance grant.

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, January 21st*, 1958.]

---

440. *Studies in the Steroid Group. Part LXXI.* The Preparation and Reactions of 9α-Methylergostane Derivatives.*

By E. R. H. JONES, G. D. MEAKINS, and J. S. STEPHENSON.

Treatment of 3β-acetoxy-9α- and -9β-Δ^7-11-ketones of the ergostane series in methyl iodide with potassium *tert.*-butoxide in *tert.*-butyl alcohol gives high yields of compounds containing a 9α-methyl group. During this process the 3-methyl ethers are formed to an appreciable extent.

Some properties of the 9α-methyl-steroids are described. The presence of this additional substituent has a profound effect on the reactions of adjacent unsaturated centres and 11-oxygen functions.

INTEREST in steroids possessing additional methyl groups at various nuclear positions has developed recently from several points of view. The original impetus for such studies was the recognition of tetracyclic triterpenes as 4 : 4 : 14-trimethyl-steroids. Degradation of lanosterol derivatives gave 14-methyl-steroids,[1,2,3] which were subsequently synthesised from steroidal materials,[4] and later cholesterol was converted into lanost-8-enol.[5] A second focus of attention is the effect of nuclear methyl groups on physiological activity: thus 2- and 6-alkyl compounds [6,7] are more potent, for example, in the glycogen deposition

* Part LXX, *J.*, 1955, 3420.

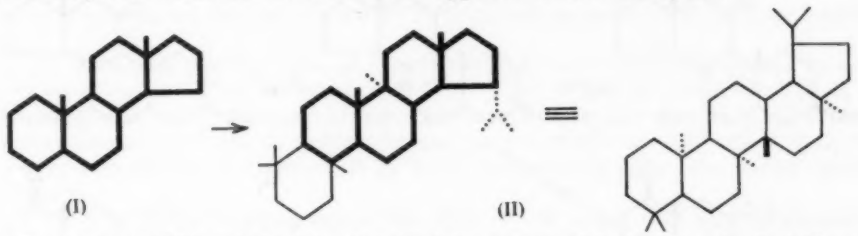
[1] Voser, White, Heusser, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1952, **35**, 830.
[2] Voser, Heusser, Jeger, and Ruzicka, *ibid.*, 1953, **36**, 299.
[3] Barton, Ives, and Thomas, *J.*, 1954, 903.
[4] Barton, Ives, Kelly, Woodward, and Patchett, *Chem. and Ind.*, 1954, 605.
[5] *Idem*, *J.*, 1957, 1131.
[6] Hogg, Lincoln, Jackson, and Schneider, *J. Amer. Chem. Soc.*, 1955, **77**, 6401; Ringold and Rosenkrantz, *J. Org. Chem.*, 1956, **21**, 1335.
[7] Spero, Thompson, Magerlein, Hanze, Murray, Sebek, and Hogg, *J. Amer. Chem. Soc.*, 1956, **78**, 6213; Ringold, Batres, and Rosenkrantz, *J. Org. Chem.*, 1957, **22**, 99.

XUM

test, than the parent hormones. Various 4-monomethyl-[8] and 4 : 4-dimethyl-steroids[9] have also been described, and the 3-methyl compounds have been used as a basis for stereochemical studies.[10]

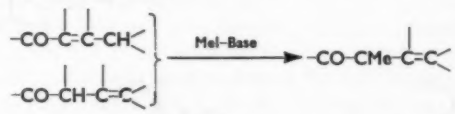
The present work is concerned with the preparation and properties of 9-methyl-steroids. Introduction of a 9-methyl group is a critical stage in a scheme for converting a steroid into the enantiomer of a pentacyclic triterpene [cf. (I) ⟶ (II)], a project of some interest in that the fundamental structures of the β-amyrin–lupeol group, although well substantiated, have not yet been finally confirmed by partial or total synthesis. The possible effects of a 9-methyl group on the biological activity of steroid hormones are also of interest, especially as other 9α-substituents[11] (notably fluorine) cause marked variations in hormone activity.

A more immediate consequence of 9-methylation is that it produces a system with methyl groups at the neighbouring positions 9 and 10, which might be expected to modify the characteristic properties normally associated with various steroidal functional groups, particularly the almost universal rule of rear approach of certain reagents.



(I) (II)

The best possibility of obtaining 9-methylation appeared to be through alkylation of an αβ- or a βγ-unsaturated 11-ketone:



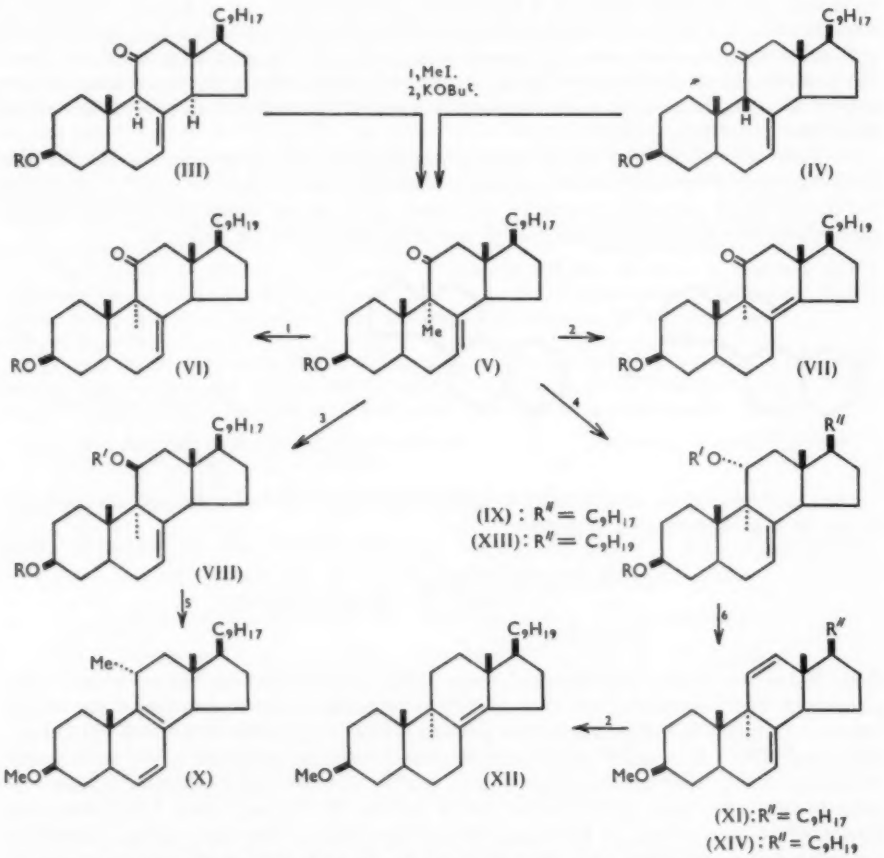
Methylation of the conjugated ketone 3β-acetoxyergost-8-en-11-one[12] was first attempted, but the results were obscured by a base-induced isomerisation of the steroid ketone. Detailed investigation (to be published later) indicated that the Δ^7-11-ketones [(III) and (IV); R = Ac][12] were more promising starting materials since, with double activation at $C_{(9)}$, they produce anions more readily than the αβ-unsaturated isomer. In order to take advantage of this factor and to prevent the derived anion from isomerising (to the Δ^8-11-keto-system) it was desirable that the anion, when once formed, should be methylated very rapidly. This was achieved by reversing the usual sequence, *i.e.*, by adding the base (potassium *tert.*-butoxide in *tert.*-butyl alcohol) to a solution of the Δ^7-11-ketone [(III) and (IV); R = Ac] in methyl iodide. After saponification of the products two 9α-methyl-Δ^7-11-ketones were isolated: the 3β-hydroxy-compound (V; R = H) in 50% yield, and the 3β-methoxy-derivative (V; R = Me) in ~17% yield.

The structures proposed for compounds based on formula (V) are supported by the following evidence. Studies of the C–H bending region of the infrared spectrum (notably bands near 1380 $cm.^{-1}$) showed that derivatives of (V) have a higher methyl group content

[8] Beton, Halsall, Jones, and Phillips, *J.*, 1957, 145; Meakins and Rodig, *J.*, 1956, 4679; Hartman, Tomasewski, and Dreiding, *J. Amer. Chem. Soc.*, 1956, **78**, 5662.
[9] Cooley, Ellis, and Petrow, *J.*, 1955, 2998; Adams, Patel, Petrow, Stuart-Webb, and Sturgeon, *J.*, 1956, 4490.
[10] Barton, Campos-Neves, and Cookson, *J.*, 1956, 3500.
[11] Fried and Sabo, *J. Amer. Chem. Soc.*, 1957, **79**, 1130; Spero, Thompson, Lincoln, Schneider, and Hogg, *ibid.*, p. 1515.
[12] Part LXII, *J.*, 1953, 2921.

XUM

than related steroidal reference compounds. Spectroscopic examination of compounds (V; R = Ac and Me) disclosed the presence of side-chain (Δ^{22}) unsaturation and a tri-substituted double bond which, from the mode of genesis of these compounds, must be placed at position 7 : 8. The stability of these Δ^7-11-ketones under alkaline conditions



which cause isomerisation of the 9-hydrogen ketones (III) and (IV) is thus strong presumptive evidence for methylation at position 9. The α-orientation of the 9-substituent is based on rotational data {compare, for example, the $[M]_D$ values of the Δ^7-11-ketones: (III; R = Ac) with 9αH, +114°; (V; R = Ac) with 9αMe, +146°; (IV; R = Ac) with 9βH, −820°}. A more powerful demonstration of this feature is provided by the rotatory dispersion curves of the acetate (V; R = Ac) and its derivatives kindly determined for us by Professor C. Djerassi.

In investigation of the chemistry of the 9α-methyl-steroids attention has been concentrated on the 7 : 8-double bond and the 11-keto-group. We had in mind the eventual removal of either or both of these features and expected to discern effects due to the 9α-methyl group. In many cases it was more convenient to work with the 3-methyl ethers

in order to avoid complications due to hydrolysis, elimination, etc., of the 3-hydroxy- or -acyloxy-group.

Hydrogenation of the acetate (V; R = Ac) with platinum in ethyl acetate affected only the $\Delta^{22:23}$-bond to give compound (VI; R = Ac), while reduction in acetic acid using a large proportion of catalyst caused simultaneous migration of the nuclear double bond, producing an isomeric dihydro-compound (VII; R = Ac). In the 9α-methyl series the $\Delta^{7} \longrightarrow \Delta^{8(14)}$ isomerisation under acidic hydrogenation conditions requires a high ratio (approximately equal weights) of catalyst to substrate: the ease of conversion may also depend on the nature of the 3-substituent. Thus reduction of the alcohols (V; R = H) and (IX; R = Me, R′ = H) with normal catalyst proportions did not bring about migration, whereas from the ether (XI) a $\Delta^{8(14)}$-compound was formed when a large proportion of catalyst was used. [The positions of nuclear unsaturation in these compounds and others described in this work follow from their spectroscopic characteristics. A useful general distinction between 11-ketones with 7 : 8- and 8 : 14-double bonds is that only the former give appreciable C=C stretching bands (near 1665 cm.$^{-1}$). The ultraviolet end-absorption data for Δ^{7}- and $\Delta^{8(14)}$-compounds are collected in the Experimental part.]

Attempts to induce migration of nuclear double bonds in 9-methyl-steroids by acid were unsuccessful. Thus, for instance, the Δ^{7}- (V; R = Bz) and the $\Delta^{8(14)}$ (VII; R = Me) compounds were unchanged after treatment with hydrogen chloride in chloroform. Similar observations with 3β-methoxy-9α-methylergost-8(14)-ene (XII) show that the 11-oxygen function is not responsible for these results, which differ from normal steroid behaviour.

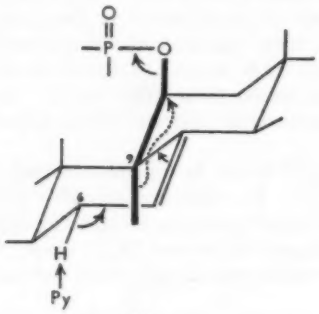
Reduction of the 11-keto-group of the ether (V; R = Me) with lithium–ammonia–ethanol and with lithium aluminium hydride gave high yields of different products which, from their methods of preparation, are formulated as the (equatorial) 11α- and (axial) 11β-epimers (IX and VIII respectively; R = Me, R′ = H). It was expected that the hydroxyl group in the latter alcohol would be very resistant to esterification.[13] However, treatment with acetic anhydride–pyridine at 20° afforded the corresponding acetate (VIII; R = Me, R′ = Ac) in 20% yield. Although acetylation of the 11β-hydroxyl group in the related 9α-hydrogen compound (ergosta-7 : 22-diene-3β : 11β-diol [13]) was not studied in detail, it appears that the 9α-methyl compound is the more reactive in this respect. Recent work with normal steroids [14] shows that an 8 : 9- or 8 : 14-double bond facilitates esterification of 11β-hydroxyl groups. The reactivity of the hydroxyl group in the Δ^{8}-compounds appears to be very similar to that found in the 9α-methyl-Δ^{7}-system.

Participation of the 9-methyl group was first met in dehydration studies with the epimeric 11-alcohols. With pyridine and phosphorus oxychloride at room temperature the 11β-alcohol (VIII; R = Me, R′ = H) gave an alkali-soluble phosphorus ester, but at 115° a dehydrated product was obtained. This contained a conjugated system ($\lambda_{max.}$ 2750 Å, ε 6150, shoulder at 2800 Å), showing that removal of the 11-hydroxyl group is accompanied by some skeletal change. Formulation (X) accommodates the similarity of the ultraviolet absorption to that of *iso*dehydrocholesterol [15] ($\lambda_{max.}$ 2710 and 2780 Å, ε 3800) and is supported by the occurrence in the infrared spectrum of a band (720 cm.$^{-1}$) corresponding to a disubstituted *cis*-double bond.[16] After the formation of a phosphorus ester from the alcohol (VIII; R = Me, R′ = H) and subsequent ionisation of this group, the 9α-methyl group is ideally placed for migration along the α-face of the molecule [see the planar arrangement of Me, $C_{(9)}$, $C_{(11)}$, and O indicated by heavy lines in the diagram (*A*)]. The rearrangement is completed by double-bond migration to supply the electron-deficiency at $C_{(9)}$, and concomitant loss of a proton (shown arbitrarily as 6α) from $C_{(6)}$.

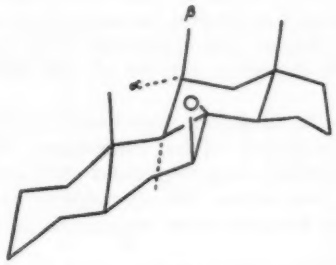
[13] Part LXV, *J.*, 1954, 731; Part LXX, *J.*, 1955, 3420.
[14] Wendler, Graber, Snoddy, and Bollinger, *J. Amer. Chem. Soc.*, 1957, **79**, 4476.
[15] Barton and Cox, *J.*, 1949, 218.
[16] Part LXVII, *J.*, 1954, 800.

The occurrence of this mode of dehydration rather than the simple alternative involving *trans*(diaxial)-elimination between 11β-OH and 12α-H is a good illustration of the well-known difficulty of forming 11 : 12-double bonds by ionic eliminations.[13]

Dehydration of the 11α-alcohol (IX; R = Me, R′ = H) with phosphorus oxychloride was much more difficult and gave small amounts of trienes (X) and (XI). The unconjugated 7 : 11 : 22-triene-ether (XI) was much better prepared by pyrolysis of the 11α-benzoate (IX; R = Me, R′ = Bz), in which there should be no rearrangement *via* ionic intermediates. The infrared spectrum of this triene-ether indicated the presence of a disubstituted (Δ^{11})-bond, so the original methylation did not occur at $C_{(12)}$ as well as at $C_{(9)}$. The related unconjugated 7 : 11-diene-ether (XIV) was prepared from the 11α-alcohol (IX;



(*A*)



(*B*)

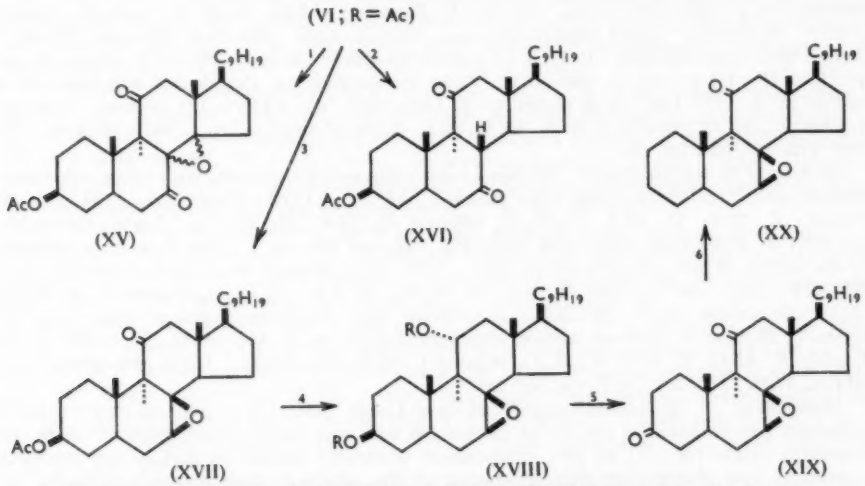
R = Me, R′ = H) by reduction of the side-chain [to give the ether (XIII; R = Me, R′ = H)], benzoylation (to XIII; R = Me, R′ = Bz), and pyrolysis. Hydrogenation of the triene-ether (XI) gave 3β-methoxy-9α-methylergost-8(14)-ene (XII), providing a method of removing the original 11-oxygen function. The double-bond migration from the 7 : 8- to the 8 : 14-position accompanying this process could presumably have been prevented by using less catalyst in the hydrogenation stage.

Oxidation of the 7 : 8-double bond was studied with the Δ^7-11-ketone (VI; R = Ac). Only the main oxidation products and their derivatives are considered here (minor, unidentified, substances are recorded in the Experimental part). The chief features of the structures assigned to these compounds are well supported by analytical and spectroscopic data: the stereochemical aspects are discussed in later paragraphs.

Oxidation of the Δ^7-11-ketone (VI; R = Ac) with chromic anhydride in acetic acid yielded three neutral products, one of which (20% yield) was almost certainly the 7 : 11-dioxo-8 : 14-oxide (XV). With hydrogen peroxide in acetic acid at 100° the ketone (VI; R = Ac) gave a small amount of the 7 : 11-diketone (XVI), and at room temperature a low yield of the 7 : 8-epoxide (XVII). The epoxide was produced quantitatively by treatment with perbenzoic acid in benzene. Refluxing the epoxide (XVII) with lithium aluminium hydride in tetrahydrofuran for 6 hours failed to open the oxide ring; the product, a diol-oxide (XVIII; R = H), was remarkable in forming a diacetate (XVIII; R = Ac) on acetylation at room temperature. Chromic acid oxidation of the diol-oxide (XVIII; R = H) afforded the corresponding dioxo-oxide (XIX), from which Wolff–Kishner reduction removed the unhindered 3-keto-group to give the 11-oxo-7 : 8-epoxide (XX).

Stereochemical uncertainty arises at $C_{(8)}$ in the 7 : 11-diketone (XVI). However, the conditions under which the compound is formed should ensure stereomutation to the more stable configuration, and an 8β(H)-structure, which allows an all-chair conformation, is to be expected.

The configuration of the epoxy-group in compound (XVII) and its derivatives is more difficult to predict. Previous oxidations of 7 : 8-double bonds in normal steroids with per-acid [17,18] are considered to give α-epoxides in accordance with the general tendency for rear approach of reagents to the steroid molecule. Application of this concept to the oxidation of the compound (VI; R = Ac) is clearly vitiated by the extra (9α-)methyl group; indeed its presence could be construed as providing *prima facie* evidence for β-attack by per-acid. A better argument can be based on the unusually ready acetylation of the 11-hydroxyl group in the derived diol oxide (XVIII; R = H). Models indicate that with an α-7 : 8-epoxide, which would have ring B in a semi-boat form, access to either



Reagents: 1, CrO_3–AcOH. 2, H_2O_2–AcOH at 100°. 3, BzO_2H–C_6H_6 or H_2O_2–AcOH at 20°. 4, $LiAlH_4$. 5, CrO_3. 6, Wolff–Kishner.

11α- or 11β-hydroxyl groups would be severely impeded. This view is supported by the behaviour of 8α-ergostane derivatives where both 11-hydroxyl groups are unreactive.[19] A β-7 : 8-oxide system can adopt an all-chair form (see Figure *B*) in which, although the 11β-hydroxyl group is again subject to severe hindrance, the corresponding 11α(equatorial)-group is relatively free. For this reason the diol oxide (XVIII; R = H) is provisionally formulated as a 3β : 11α-dihydroxy-7β : 8β-epoxide. The β-epoxide configuration will, of course, also apply to (XVII), (XIX), and (XX).

The 7 : 8-double bond of compound (VI; R = Ac) did not react with osmium tetroxide even under conditions in which other unreactive bonds were attacked.[20] This is in accordance with the greater steric requirements of osmium tetroxide than of perbenzoic acid, and with the hindrance by methyl groups on both faces of the 9α-methyl-steroid molecule.

Experimental

M. p.s were determined on a Kofler block and are corrected. Rotations were determined for $CHCl_3$ solutions at room temperature. Peter Spence alumina (grades O and H) was used for chromatography: deactivated alumina was prepared by treating grade H material with 5% (by volume) of 10% aqueous acetic acid. Light petroleum refers to the fraction with b. p.

[17] Alt and Barton, *J.*, 1954, 1356.
[18] Grigor, Laird, Maclean, Newbold, and Spring, *J.*, 1954, 2333; Grigor, Newbold, and Spring, *J.*, 1955, 1170.
[19] Bream, Eaton, and Henbest, *J.*, 1957, 1974.
[20] Castells and Meakins, *Chem. and Ind.*, 1956, 248.

60—80°. Ultraviolet spectra were determined for EtOH solutions with a Unicam spectrometer. Infrared spectra were recorded on a Perkin-Elmer model 21 double-beam instrument, carbon disulphide solutions being used unless stated otherwise.

Methylation of 3β-*Acetoxy*-9β-*ergosta*-7 : 22-*dien*-11-*one* (IV; R = Ac).—A M-solution of potassium *tert.*-butoxide in *tert.*-butyl alcohol (215 c.c.) was added quickly to a stirred solution of the ketone [11] (3 g.) in methyl iodide (70 c.c.) at 20°. After 20 min. the mixture was poured into water, and the material isolated by ether-extraction was refluxed with 10% ethanolic potassium hydroxide (150 c.c.) for 4 hr. under nitrogen. Standard manipulation gave a mixture (2·7 g.) which was adsorbed from light petroleum–benzene (10 : 1) on deactivated alumina (200 g.). Light petroleum–benzene (4 : 1; 3 l.) eluted material (513 mg.) which crystallised from methanol to give 3β-*methoxy*-9α-*methylergosta*-7 : 22-*dien*-11-*one* (V; R = Me) (400 mg.), m. p. 130—132·5°, $[\alpha]_D$ +47° (*c* 1·1) (Found: C, 82·05; H, 10·9. $C_{30}H_{48}O_2$ requires C, 81·8; H, 11·0%). Light absorption: $\nu_{max.}$ 3014 sh, 1705, 1668, 973, 825, and 795 cm.$^{-1}$. Elution with benzene–ether (10·1; 1 l.) yielded 3β-*hydroxy*-9α-*methylergosta*-7 : 22-*dien*-11-*one* (V; R = H) (1·4 g.), m. p. 160—163°. After recrystallisation the alcohol was obtained as needles, m. p. 161—164°, or as plates, m. p. 165—169°, $[\alpha]_D$ +51° (*c* 1·0) (Found: C, 81·45; H, 10·8. $C_{29}H_{46}O_2$ requires C, 81·6; H, 10·9%). Light absorption: $\nu_{max.}$ 3617, 3014 sh, 1703, 1665, 972, 820, and 795 cm.$^{-1}$.

3β-*Acetoxy*-9α-*methylergosta*-7 : 22-*dien*-11-*one* (prepared by treatment with acetic anhydride–pyridine at 20° and crystallised from ethanol) had m. p. 133·5—134·5°, $[\alpha]_D$ +31° (*c* 0·85) (Found: C, 79·2; H, 10·2. $C_{31}H_{48}O_3$ requires C, 79·4; H, 10·3%). Light absorption: $\nu_{max.}$ 3017 sh, 1735, 1705, 1662, 1246, 1028, 972, 825, and 800 cm.$^{-1}$. The 3β-*benzoate*, obtained by the action of benzoyl chloride–pyridine at 20°, crystallised from ethanol as needles, m. p. 207—212°, $[\alpha]_D$ +35° (*c* 0·98) (Found: C, 81·45; H, 9·6. $C_{36}H_{50}O_3$ requires C, 81·45; H, 9·6%). Oxidation of the 3β-alcohol in acetone with 8N-chromic acid yielded 9α-*methylergosta*-7 : 22-*diene*-3 : 11-*dione*, needles (from methanol), m. p. 156—158°, $[\alpha]_D$ +63° (*c* 0·9) (Found: C, 81·8; H, 10·5. $C_{29}H_{44}O_2$ requires C, 82·0; H, 10·4%). Light absorption: $\nu_{max.}$ 3014 sh, 1720, 1710, 1667, 972, and 825 cm.$^{-1}$.

Methylation of 3β-*Acetoxyergosta*-7 : 22-*diene*-11-*one* (III; R = Ac).—A M-solution of potassium *tert.*-butoxide in *tert.*-butyl alcohol (86 c.c.) was added to the ketone [11] (500 mg.) in methyl iodide (28 c.c.) at 20°. Subsequent treatment similar to that of the preceding experiment and chromatographic separation of the products gave 3β-methoxy-9α-methylergosta-7 : 22-dien-11-one (90 mg.), m. p. 128—130°, $[\alpha]_D$ +46° (*c* 1·1), and 3β-hydroxy-9α-methylergosta-7 : 22-dien-11-one (250 mg.), m. p. 161—163°, $[\alpha]_D$ +48° (*c* 0·9).

3β-*Acetoxy*-9α-*methylergost*-7-*en*-11-*one* (VI; R = Ac).—A solution of 3β-acetoxy-9α-methylergosta-7 : 22-dien-11-one (1 g.) in ethyl acetate (50 c.c.) was shaken in hydrogen with Adams catalyst (500 mg.) until hydrogenation ceased (uptake 1 mol.). The residue obtained after removal of catalyst and solvent crystallised from methanol, to give the *keto-acetate* as needles (0·82 g.), m. p. 125·5—127·5°, $[\alpha]_D$ +43° (*c* 0·85) (Found: C, 79·05; H, 10·8. $C_{31}H_{50}O_3$ requires C, 79·1; H, 10·7%). Light absorption: $\nu_{max.}$ 3014 sh, 1735, 1705, 1667, 1241, 1027, 825, and 800 cm.$^{-1}$

3β-*Hydroxy*-9α-*methylergost*-7-*en*-11-*one* (VI; R = H).—A solution of the corresponding 7 : 22-dienol (102 mg.) in ethyl acetate (4 c.c.) was hydrogenated in the presence of prereduced Adams catalyst (50 mg.) for 1 hr. More catalyst (100 mg.) was added and the shaking was continued for a further hour. The *keto-alcohol*, isolated in the usual way, crystallised from methanol as needles (90 mg.), m. p. 168—170°, $[\alpha]_D$ +53° (*c* 0·98) (Found: C, 81·1; H, 11·25. $C_{29}H_{46}O_2$ requires C, 81·25; H, 11·3%). Light absorption: $\nu_{max.}$ 3595, 3022 sh, 1701, 1663, 1037, 810, and 794 cm.$^{-1}$.

3β-*Acetoxy*-9α-*methylergost*-8(14)-*en*-11-*one* (VII; R = Ac).—A solution of 3β-acetoxy-9α-methylergosta-7 : 22-dien-11-one (100 mg.) in acetic acid (8 c.c.) was shaken in hydrogen with Adams catalyst (100 mg.) for 7 hr. Standard manipulation gave the *keto-acetate*, needles (from methanol), m. p. 136—137·5°, $[\alpha]_D$ +104° (*c* 0·95) (Found: C, 79·0; H, 10·75. $C_{31}H_{50}O_3$ requires C, 79·1; H, 10·7%). Light absorption: $\nu_{max.}$ 1730, 1705, 1241, and 1028 cm.$^{-1}$.

Isomerisation of the 7 : 8-double bond appears to depend on the ratio of catalyst to substrate and possibly on the nature of the 3-substituent. Thus hydrogenation of 3β-hydroxy-9α-methylergosta-7 : 22-dien-11-one (2 g.) in acetic acid (50 c.c.) in the presence of Adams catalyst (0·5 g.) for 6 hr. yielded 3β-hydroxy-9α-methylergost-7-en-11-one (1·2 g.), m. p. 168—170°.

3β-*Hydroxy*-9α-*methylergost*-8(14)-*en*-11-*one* (VII; R = H).—Hydrolysis of the foregoing

XUM

acetate (1·07 g.) with 10% ethanolic potassium hydroxide gave the *keto-alcohol* (0·9 g.) which crystallised from aqueous methanol as plates, double m. p. 65—70° and 106—109°, $[\alpha]_D$ +130° (*c* 0·85) (Found: C, 81·05; H, 11·25. $C_{29}H_{48}O_2$ requires C, 81·25; H, 11·3%). Light absorption: $\nu_{max.}$ 3570, 1705, and 1040 cm.$^{-1}$. The 3 : 5-dinitrobenzoate (not analysed) of the alcohol had m. p. 182·5°, $[\alpha]_D$ +71° (*c* 1·1). Treatment of the alcohol with benzoyl chloride–pyridine at 20° gave the *benzoate* which crystallised from methanol, double m. p. 127—129° and 136—138°, $[\alpha]_D$ +92° (*c* 0·95) (Found: C, 80·75; H, 9·95. $C_{36}H_{52}O_3$ requires C, 81·15; H, 9·8%).

Attempted Isomerisation of Δ^7- *and* $\Delta^{8(14)}$-9α-*Methyl Compounds under Acidic Conditions.*—(*a*) A stream of dry hydrogen chloride was passed for 2 hr. through a solution of 3β-benzoyloxy-9α-methylergosta-7 : 22-dien-11-one (V; R = Bz) (500 mg.) in chloroform (20 c.c.) at −30°. The solution was diluted with ether, stirred with sodium hydrogen carbonate for 30 min., and poured into water. The material isolated from the ether layer crystallised from ethanol to give material (400 mg.), $[\alpha]_D$ +38° (*c* 1·0), m. p. 208—212° undepressed on admixture with starting material

3β-Benzoyloxy-9α-methylergost-8(14)-en-11-one (VII; R = Bz) and 3β-methoxy-9α-methylergost-8(14)-ene (XII) were also unchanged by treatment under these conditions.

(*b*) Hydrogen chloride was passed for 2 hr. through a solution of 3β-acetoxy-9α-methylergost-7-en-11-one (VI; R = Ac) (100 mg.) in acetic acid (40 c.c.) at 20°, and the mixture was kept for 3 days. Removal of solvent under reduced pressure and crystallisation of the residue from methanol afforded starting material (90 mg.), m. p. 125—127°.

(*c*) A solution of 3β-methoxy-9α-methylergost-8(14)-ene (XII) (0·5 g.) in a mixture of chloroform (5 c.c.), acetic acid (10 c.c.), and 10N-hydrochloric acid (2 c.c.) was boiled for 2 hr. Spectroscopic examination of the fractions obtained by chromatography of the product showed the absence of Δ^{14}-compounds: none of the fractions crystallised.

3β-*Methoxy*-9α-*methylergosta*-7 : 22-*dien*-11β-*ol* (VIII; R = Me, R′ = H).—A stirred solution of 3β-methoxy-9α-methylergosta-7 : 22-dien-11-one (1·2 g.) in dry ether (100 c.c.) was refluxed with lithium aluminium hydride (0·4 g.) for 1 hr. After the addition of ethyl acetate and then dilute sulphuric acid the product was isolated with ether. Crystallisation from methanol gave the *alcohol* (0·91 g.) as plates, m. p. 137—139°, $[\alpha]_D$ −54° (*c* 1·0) (Found: C, 81·4; H, 11·55. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%). Light absorption: $\nu_{max.}$ 3642, 1657, 1102, 972, 818, and 798 cm.$^{-1}$.

Acetylation of 3β-*Methoxy*-9α-*methylergosta*-7 : 22-*dien*-11β-*ol* (VIII; R = Me, R′ = H).—A solution of the alcohol (300 mg.) in acetic anhydride–pyridine (1 : 1; 40 c.c.) was kept at 20° for 15 hr. Dilution with water, extraction with ether, and removal of solvents *in vacuo* yielded material (280 mg.) which was adsorbed from light petroleum (5 c.c.) on deactivated alumina (100 g.). The fraction (60 mg.) eluted with light petroleum–benzene (2 : 1; 150 c.c.) crystallised from methanol, to give 11β-*acetoxy*-3β-*methoxy*-9α-*methylergosta*-7 : 22-*diene*, m. p. 123—125°, $[\alpha]_D$ −27° (*c* 0·8) (Found: C, 79·2; H, 10·7. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%). Light absorption: $\nu_{max.}$ 1728, 1683, 1239, 1100, 1019, and 980 cm.$^{-1}$. Further elution with the same solvent mixture (300 c.c.) gave starting material (180 mg.), m. p. 136·5—137·5° after crystallisation from methanol.

Dehydration of 3β-*Methoxy*-9α-*methylergosta*-7 : 22-*dien*-11β-*ol* (VIII; R = Me, R′ = H).—A solution of the alcohol (100 mg.) in pyridine (30 c.c.) was boiled with phosphorus oxychloride (3 c.c.) for 2 hr. under nitrogen, and then poured on ice. The material isolated by ether-extraction was chromatographed on alumina (10 g.; Grade 0). The fraction (68 mg.) eluted with light petroleum (250 c.c.) crystallised from acetone–methanol to give a product considered to be 3β-*methoxy*-11α-*methylergosta*-6 : 8 : 22-*triene* (X), m. p. 76—78°, $[\alpha]_D$ −21° (*c* 0·5) (Found: C, 84·55; H, 11·4. $C_{30}H_{48}O$ requires C, 84·8; H, 11·4%). Light absorption: $\lambda_{max.}$ 2750 Å (ε 6150), 2800 Å sh; $\nu_{max.}$ 3020 sh, 1102, 973, and 720 cm.$^{-1}$.

3β-*Methoxy*-9α-*methylergosta*-7 : 22-*dien*-11α-*ol* (IX; R = Me, R′ = H).—Lithium (0·6 g.) was added to a stirred solution of 3β-methoxy-9α-methylergosta-7 : 22-dien-11-one (1·53 g.) in ether (60 c.c.) and liquid ammonia (60 c.c.). After 30 min. absolute ethanol was added slowly until the blue colour disappeared. The ammonia was allowed to evaporate and water was added. Isolation with ether and crystallisation from methanol gave the *alcohol* (1·2 g.), m. p. 113—120°, which on recrystallisation had m. p. 125—126°, $[\alpha]_D$ −33° (*c* 1·0) (Found: C, 81·5; H, 11·3. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%). Light absorption: $\nu_{max.}$ 3636, 3006 sh, 1100, 972, 818, and 794 cm.$^{-1}$.

Treatment of this product (747 mg.) in pyridine (50 c.c.) with benzoyl chloride (5 c.c.) at

XUM

100° for 12 hr. gave 11α-*benzoyloxy*-3β-*methoxy*-9α-*methylergosta*-7 : 22-*diene* (670 mg.), m. p. 197—203° (from methanol), $[\alpha]_D$ −63° (*c* 1·1) (Found: C, 81·0; H, 10·0. $C_{37}H_{54}O_3$ requires C, 81·3; H, 9·95%).

3β-*Methoxy*-9α-*methylergost*-7-*en*-11α-*ol* (XIII; R = Me, R′ = H).—A solution of 3β-methoxy-9α-methylergosta-7 : 22-dien-11α-ol (3 g.) in acetic acid (400 c.c.) was shaken in hydrogen with Adams catalyst (0·5 g.) for 15 hr. The solution was filtered and diluted with water, and the product was collected. Two crystallisations from methanol gave the *alcohol* (2·21 g.), m. p. 156—157°, $[\alpha]_D$ −22° (*c* 0·9) (Found: C, 80·8; H, 11·6. $C_{30}H_{52}O_2$ requires C, 81·0; H, 11·8%). Light absorption: $\nu_{max.}$ 3616, 3027 sh, 1095, 995, 813, and 790 cm.$^{-1}$.

The 11α-alcohol (1·84 g.) in pyridine (50 c.c.) was treated with benzoyl chloride (10 c.c.) and kept at 50° for 2 hr. and then at 20° for 12 hr. Standard manipulation followed by crystallisation from ethyl acetate gave the 11α-*benzoyloxy-compound* (1·98 g.), m. p. 198—202°, $[\alpha]_D$ −6° (*c* 1·1) (Found: C, 80·9; H, 10·4. $C_{37}H_{56}O_3$ requires C, 81·0; H, 10·3%).

Pyrolysis of 11α-*Benzoates*.—(*a*) A Pyrex-glass tube (½″ internal diameter) containing 11α-benzoyloxy-3β-methoxy-9α-methylergosta-7 : 22-diene (117 mg.) was evacuated and flushed out with nitrogen several times, and then heated at 300°/20 mm. for 1 hr. The mixture was treated with ethanol, in which part of it (largely benzoic acid) dissolved. After the addition of excess of 0·01N-aqueous sodium hydroxide the mixture was titrated with 0·01N-hydrochloric acid. (The figures showed that the elimination had proceeded to the extent of 90%.) Dilution with water and extraction with ether was followed by chromatography of the product on alumina (15 g.; Grade 0). Light petroleum–benzene (50 : 1; 400 c.c.) eluted 3β-*methoxy*-9α-*methylergosta*-7 : 11 : 22-*triene* (XI) (64 mg.), m. p. 138—139° (needles from methanol), $[\alpha]_D$ −27° (*c* 0·95) (Found: C, 84·75; H, 11·6. $C_{30}H_{48}O$ requires C, 84·8; H, 11·4%). Light absorption: $\nu_{max.}$ 3007 sh, 1102, 973, and 745 cm.$^{-1}$.

(*b*) Pyrolysis of 11α-benzoyloxy-3β-methoxy-9α-methylergost-7-ene by the same method gave 3β-*methoxy*-9α-*methylergosta*-7 : 11-*diene* (XIV), m. p. 125—126° (from methanol), $[\alpha]_D$ −11° (*c* 1·05) (Found: C, 84·6; H, 11·6. $C_{30}H_{50}O$ requires C, 84·4; H, 11·8%). Light absorption: $\nu_{max.}$ 3007 sh, 1100, 797, and 744 cm.$^{-1}$.

3β-*Methoxy*-9α-*methylergost*-8(14)-*ene* (XII).—3β-Methoxy-9α-methylergosta-7 : 11 : 22-triene (250 mg.) in acetic acid (50 c.c.) was shaken in hydrogen with Adams catalyst (246 mg.) for 15 hr. The product isolated in the usual way was adsorbed from light petroleum on alumina (35 g.; Grade 0). Light petroleum–benzene (33 : 1) eluted material (240 mg.) which on crystallisation from acetone–methanol gave the *tetrahydro-compound* as needles, m. p. 53·5—55·5°, $[\alpha]_D$ +25° (*c* 0·83) (Found: C, 84·0; H, 12·2. $C_{30}H_{52}O$ requires C, 84·0; H, 12·2%). Light absorption: ε_{2100} 9700, ε_{2200} 3000; $\nu_{max.}$ 1102 cm.$^{-1}$.

Oxidation of 3β-*Acetoxy*-9α-*methylergost*-7-*en*-11-*one* (VI; R = Ac).—(a) *With chromium trioxide in acetic acid.* Chromium trioxide (450 mg.) was added to a solution of the Δ^7-11-ketone (600 mg.) in acetic acid (20 c.c.), and the mixture was stirred at 60° for 4 hr. Dilution with water and extraction with ether gave a gum (550 mg.) which was adsorbed from light petroleum–benzene (2 : 1, 30 c.c.) on alumina (100 g.; Grade 0). Elution with benzene–ether (19 : 1, 600 c.c.) afforded a *compound* (100 mg.) of unknown structure which, crystallised from methanol, had m. p. 183—185°, $[\alpha]_D$ +46° (*c* 0·71) (Found: C, 76·2, 76·6; H, 10·0, 10·2%). Light absorption: $\lambda_{max.}$ 2320 Å (ε 8700); $\nu_{max.}$ 1735, 1709, 1678, 1625, 1239, 1036, and 900 cm.$^{-1}$. Benzene–ether (9 : 1; 600 c.c.) afforded a second compound (120 mg.) which was almost certainly 3β-*acetoxy*-8ξ : 14ξ-*epoxy*-9α-*methylergostane*-7 : 11-*dione* (XV), m. p. 184—186° (from methanol), $[\alpha]_D$ +34° (*c* 0·75) (Found: C, 74·4; H, 9·7. $C_{31}H_{48}O_5$ requires C, 74·4; H, 9·7%). Light absorption: $\nu_{max.}$ 1735, 1725, 1702, 1239, 1028, and 901 cm.$^{-1}$; no selective absorption in the ultraviolet. Benzene–ether (4 : 1; 500 c.c.) eluted a third substance (55 mg.) (of unknown structure), m. p. 165—169° (from methanol), $[\alpha]_D$ +152° (*c* 0·75). Light absorption: $\lambda_{max.}$ 2490 Å (ε 8500); $\nu_{max.}$ 1735, 1715, 1651, 1239, 1026, 977, and 903 cm.$^{-1}$.

(b) *With hydrogen peroxide–acetic acid at* 20°. Aqueous hydrogen peroxide (0·3 c.c. of 100-vol. reagent) was added to a solution of the Δ^7-11-ketone (80 mg.) in acetic acid (4 c.c.). After 15 hr. at 20° water was added and the product was collected by filtration, dried, and adsorbed from light petroleum (3 c.c.) on deactivated alumina (10 g.). Elution with light petroleum–benzene (2 : 1; 50 c.c.) gave starting material (62 mg.). Benzene (20 c.c.) eluted a fraction (10 mg.) which proved to be 3β-acetoxy-7β : 8β-epoxy-9α-methylergostan-11-one, m. p. and mixed m. p. with an authentic specimen (described below), 135—137°.

(c) *With hydrogen peroxide–acetic acid at* 100°. A mixture of aqueous hydrogen peroxide

(0·6 c.c. of 100-vol. reagent) and acetic acid (0·6 c.c.) was added during 15 min. to a solution of the Δ^7-11-ketone (150 mg.) in acetic acid (6 c.c.) at 100°. After 2 hr. at 100° more hydrogen peroxide (0·6 c.c.; 100-vol.) was added and the heating was continued for a further 2 hr. The product, isolated by dilution with water and extraction with ether, was adsorbed from light petroleum–benzene (3 : 2; 7 c.c.) on deactivated alumina (20 g.). Elution with light petroleum–benzene (1 : 1; 100 c.c.) gave material (8 mg.), m. p. 178—180° (from methanol). From its infrared spectrum ($\nu_{max.}$ 1740, 1723, 1709, 1239, and 1026 cm.$^{-1}$) and lack of selective ultraviolet absorption, this compound is assumed to be 3β-acetoxy-9α-methylergostane-7 : 11-dione (XVI). The later fractions, eluted with more polar solvents, did not crystallise.

(d) *With perbenzoic acid.* Perbenzoic acid (20 c.c. of an 0·25M-solution in benzene) was added to the Δ^7-11-ketone (2 g.) in benzene (40 c.c.), and the mixture was left in the dark at 20° for 15 hr. After the removal of acidic material with dilute alkali the benzene solution was washed with water, dried, filtered, and evaporated *in vacuo*. Crystallisation of the residue from methanol gave 3β-*acetoxy*-7β : 8β-*epoxy*-9α-*methylergostan*-11-*one* (XVII) (1·94 g.), m. p. 134—136°. The pure product obtained by a further crystallisation from methanol had m. p. 138—139·5°, $[\alpha]_D$ −15° (*c* 1·0) (Found: C, 76·25; H, 10·3. $C_{31}H_{50}O_4$ requires C, 76·5; H, 10·4%). Light absorption: $\nu_{max.}$ 1730, 1690, 1245, and 1030 cm.$^{-1}$.

7β : 8β-*Epoxy*-9α-*methylergostane*-3β : 11α-*diol* (XVIII; R = H).—The foregoing epoxy-ketone (1 g.) in ether (100 c.c.) was refluxed with lithium aluminium hydride (1 g.) for 1 hr. The excess of reagent was decomposed with ethyl acetate, water was added, and the mixture was stirred for 30 min. (The use of mineral acid at this stage was avoided in order to exclude the possibility of acid-catalysed opening of the oxide ring.) Ether-extraction gave a product which was adsorbed from benzene (30 c.c.) on deactivated alumina (100 g.). Benzene–ether (4 : 1; 800 c.c.) eluted the *diol* (745 mg.; laths from methanol), m. p. 196—197°. Recrystallisation gave material, m. p. 200—207°, $[\alpha]_D$ −7° (*c* 1·0) (Found: C, 78·0; H, 11·5. $C_{29}H_{50}O_3$ requires C, 78·0; H, 11·3%). Light absorption: $\nu_{max.}$ (in Nujol) 1031, 976, and 922 cm.$^{-1}$. Repetition of this experiment with tetrahydrofuran as solvent and a reflux time of 6·5 hr. gave the same result.

3β : 11α-*Diacetoxy*-7β : 8β-*epoxy*-9α-*methylergostane* (XVIII; R = Ac).—A solution of the above diol (480 mg.) in pyridine (20 c.c.) and acetic anhydride (15 c.c.) was kept at 20° for 15 hr. and then poured slowly into ice-water. The material isolated with ether was adsorbed from light petroleum (20 c.c.) on deactivated alumina (50 g.). Elution with light petroleum–benzene (1 : 1; 30 c.c.) and crystallisation from methanol gave a product (440 mg.), m. p. 165—167°. Recrystallisation afforded the *diacetate* as needles, m. p. 165·5—167·5°, $[\alpha]_D$ −6° (*c* 1·1) (Found: C, 74·5; H, 10·5. $C_{33}H_{54}O_5$ requires C, 74·7; H, 10·3%). Light absorption: $\nu_{max.}$ no OH band, 1740, 1239, 1026, 977, 922, and 888 cm.$^{-1}$. The compound gave no colour with tetranitromethane.

7β : 8β-*Epoxy*-9α-*methylergostane*-3 : 11-*dione* (XIX).—8N-Chromic acid was added dropwise to a solution of the preceding diol (595 mg.) in acetone (100 c.c.) until the supernatant liquid remained yellow. The mixture was poured into water and extracted with ether. The material (571 mg.) so obtained was adsorbed from light petroleum (15 c.c.) on deactivated alumina (100 g.). Light petroleum–benzene (2 : 3; 900 c.c.) eluted a fraction (473 mg.) which crystallised from methanol to give the *dione*, m. p. 121—122·5°, $[\alpha]_D$ +7° (*c* 0·97) (Found: C, 78·8; H, 10·6. $C_{29}H_{46}O_3$ requires C, 78·7; H, 10·5%). Light absorption: $\nu_{max.}$ 1723, 1697, 969, and 919 cm.$^{-1}$.

7β : 8β-*Epoxy*-9α-*methylergostan*-11-*one* (XX).—A solution of the above epoxy-3 : 11-diketone (300 mg.) and 90% hydrazine hydrate (5 c.c.) in diethylene glycol (125 c.c.) was heated at 100° for 30 min., and then refluxed gently for 1 hr. Potassium hydroxide (1 g.) was added and the mixture was distilled slowly until the temperature of the solution reached 220°. The mixture was refluxed for 4 hr., cooled, and poured into dilute hydrochloric acid, and the whole was extracted with ether. The ether solution was washed with water, dried, and evaporated, and the residue (279 mg.) was chromatographed on alumina (50 g.; Grade 0). Light petroleum (250 c.c.) eluted a gum (30 mg.; $\nu_{max.}$ 1705 cm.$^{-1}$). Light petroleum–benzene (9 : 1; 800 c.c.) eluted a fraction (238 mg.) which crystallised from methanol, to give the *keto-oxide*, m. p. 88—90°, $[\alpha]_D$ −26° (*c* 1·1) (Found: C, 81·1; H, 11·3. $C_{29}H_{46}O_2$ requires C, 81·25; H, 11·3%). Light absorption: $\nu_{max.}$ 1694, 969, and 823 cm.$^{-1}$.

Ultraviolet End-absorption of Δ^7- *and* $\Delta^{8(14)}$-*Compounds.*—The data for some of the substances

described in this section are collected in the Table. The figures confirm the expectation [21] that compounds containing tetrasubstituted 8 : 14-bonds absorb much more intensely in the 2050—2200 Å region than those with trisubstituted 7 : 8-double bonds.

Δ^{7}-*Compounds*

Substituents			Double bonds	ε_{2100}	ε_{2150}	ε_{2200}
3β	9α	11	—	—	—	—
AcO	Me	=O	7	2900	1300	800
AcO	Me	=O	7 : 22	2200	1000	250
MeO	Me	HO-α	7	2000	600	100
MeO	Me	—	7 : 11 : 22	3600	300	10

$\Delta^{8(14)}$-*Compounds*

Substituents			Double bonds	ε_{2100}	ε_{2150}	ε_{2200}
AcO	H	=O	8(14)	9350	6580	2870
AcO	H	HO-β	8(14)	10,000	8700	—
AcO	H	=O	8(14) : 22	11,800	8000	3580
AcO	Me	=O	8(14)	6600	3200	2000
MeO	H	—	8(14)	10,000	5000	2600
MeO	Me	—	8(14)	9700	6000	3000

The authors are indebted to the Department of Scientific and Industrial Research for a grant (to J. S. S.), to Miss W. Peadon for recording the spectroscopic data, and to Mr. E. S. Morton for performing the microanalyses.

THE UNIVERSITY, MANCHESTER, 13.
THE DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, November 19th*, 1957.]

[21] Bladon, Henbest, and Wood, *J.*, 1952, 2737.

---

441. *The Oxidation of the Trisdipyridylosmium*(II) *Ion by the Peroxydisulphate Ion in Aqueous Solution.*

By D. H. IRVINE.

The oxidation of the trisdipyridylosmium(II) by the peroxydisulphate ion follows second-order kinetics up to about 45—50% of reaction. The breakdown of second-order kinetics probably arises through participation in the reaction of the sulphate radical produced in the primary step. The velocity constant of the reaction is given by the expression $k_0 = 2{\cdot}8 \times 10^8 \exp(-9400/RT)$. An explanation is given for the lower values of the A and E factors than with the corresponding ferrous-ion oxidation. The reaction is speeded up by hydrogen ions, chloride ions, and sulphate ions. It is suggested that this is due to the participation of a conjugate acid species in the former case, and of ion-pair complexes in the latter cases.

FEW oxidation–reduction reactions involving complex ions have been studied kinetically in detail. Such reactions are invariably too fast for ordinary kinetic investigations, particularly if the oxidation–reduction process involves only the transfer of a single electron.[1] Such reactions, if they could be studied, would undoubtedly yield valuable data on oxidation–reduction processes in solution, especially in respect to the factors governing their speed. Some attempt has been made to explain theoretically the observed difference in rates between electron-transfer reactions in solution involving complex ions and those involving simple aquated ions.[2] The theory, however, does not explain why single-electron-transfer reactions involving complex ions are fast irrespective of the nature and magnitude of the charges in the reacting species (see also ref. 1). Further, the rate of oxidation of the trisdipyridylruthenium(II) ion [1] by ceric ion is too fast to be measured in aqueous perchloric acid but is measurable in aqueous sulphuric acid. This observation led George and Irvine [1] to suggest that a small, favourable free-energy or heat change may greatly increase the rate of electron exchange. It seems probable that an explanation in terms of free-energy or heat-change difference might also account for the fact that thallic ion oxidises the trisdipyridylosmium(II) ion reversibly at a reasonable rate but does not oxidise the tris-*o*-phenanthrolineiron(II) ion reversibly, or, if it does so, the rate is extremely slow.[3]

[1] George and Irvine, *J.*, 1954, 587.
[2] Zwolinski, Marcus, and Eyring, *Chem. Rev.*, 1955, **55**, 157.
[3] Irvine, *J.*, 1957, 1841.

XUM

In a more recent theory Marcus [4] concluded that it is the standard free-energy change of the redox step and not the overall free energy which is important in determining the speed of electron-transfer reactions. He also showed that other factors which affect the rate of such reactions are the Coulombic interaction of the ionic charges of the reactants and the solvation of the charged reactants. The theory will account for the different speeds of many electron-transfer reactions [4] but many more results are clearly needed for such reactions for further testing of such a theory.

While one-electron-transfer reactions involving complex ions are nearly always fast there are examples of slow reactions in which a complex ion is oxidised by a two-electron oxidant. Such reactions might help to answer some of the above problems.

In looking for reactions of this kind which could be investigated kinetically we found that both hydrogen peroxide and the peroxydisulphate ion oxidised the trisdipyridylosmium(II) ion. Preliminary experiments having indicated that the reaction with hydrogen peroxide was more complicated, we first examined the peroxydisulphate reaction. The choice of the trisdipyridylosmium(II) ion was based on its favourable redox potential [5] and its remarkable stability in solution.[6]

The oxidation of the trisdipyridylosmium(II) ion [$Os(dipy)_3^{2+}$] by the peroxydisulphate ion ($S_2O_8^{2-}$) initially follows second-order kinetics, but departs from them after about 45—50% of reaction. This is illustrated in Fig. 1, where a = initial concentration of $Os(dipy)_3^{2+}$, b = initial concentration of $S_2O_8^{2-}$, and x is the amount of $S_2O_8^{2-}$ which is reduced in time t. A check on the stoicheiometry of the reaction showed that 1 mole of $S_2O_8^{2-}$ oxidised only 1·5 moles of $Os(dipy)_3^{2+}$ instead of the 2·0 moles expected. Since there was no evidence of equilibrium or of any destruction of the $Os(dipy)_3^{2+}$ ion (the latter was completely recoverable at the end of a kinetic run by addition of a suitable reducing agent) the result implies that some $S_2O_8^{2-}$ was used in secondary reactions. Change of concentration of $S_2O_8^{2-}$ hardly affected the stage at which departure from second-order kinetics occurred. This suggests that it is not reactions involving the $S_2O_8^{2-}$ ion as such which are responsible for the breakdown of second-order kinetics; possibly the primary step in the oxidation involves the production of the sulphate radical, *viz.*:

$$Os(dipy)_3^{2+} + S_2O_8^{2-} \longrightarrow Os(dipy)_3^{3+} + SO_4^{-} + SO_4^{2-} \quad . \quad . \quad . \quad (1)$$

and there is then competition for this radical between $Os(dipy)_3^{2+}$ on the one hand and traces of reducing matter or water itself on the other. Reaction (1) is analogous to that suggested for the oxidation of ferrous ion by peroxydisulphate.[7, 8]

Dependence of the Rate of Reaction on Ionic Strength and Temperature.—The rate was measured at 25·5°, 18·0°, and 10·2° c under various conditions of ionic strength, which was changed by adding sodium perchlorate. The results are illustrated in Fig. 2, the slopes being 3·60, 3·50, and 3·10 respectively. These values are in fair agreement with the theoretical value of 4·0 expected for a reaction between oppositely-charged bivalent ions, and is good evidence that the rate-determining step involves the species $Os(dipy)_3^{2+}$ and $S_2O_8^{2-}$.

Extrapolation of the $\sqrt{I}$ plots to zero ionic strength gives values for k_0, the true velocity constant, of 52·0, 33·8, and 22·7 l. mole^{-1} sec.$^{-1}$ at 25·5°, 18·0°, and 10·2° respectively. A plot of $\log_{10} k_0$ against $1/T$ yields

$$k_0 = 2{\cdot}8 \times 10^8 \exp(-9400/RT) \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

The corresponding value for the ferrous ion oxidation is

$$k_0 = 1 \times 10^{11} \exp(-12{,}100/RT) \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

[4] Marcus, *J. Chem. Phys.*, 1957, **26**, 867.
[5] Barnes, Dwyer, and Gyarfas, *Trans. Faraday Soc.*, 1952, **48**, 269.
[6] Burstall, Dwyer, and Gyarfas, *J.*, 1950, 953.
[7] Fordham and Leverne Williams, *J. Amer. Chem. Soc.*, 1951, **73**, 4855.
[8] Kolthoff, Medalia, and Raaen, *J. Amer. Chem. Soc.*, 1951, **73**, 1733.

XUM

The smaller value of the A factor for the reaction involving the complex ion is presumably, in terms of Zwolinski, Marcus, and Eyring's [2] picture, a consequence of the smaller degree of rearrangement of the hydration sphere required by the complex ions. A value as low as 10^8 is, however, unusual for a reaction of this charge type where values between 10^{13} and 10^{19} are normally expected.[9] The low value may be characteristic of reactions involving complex ions but there are insufficient data to confirm this.

The activation energy for the reaction involving the complex ion is also smaller than that for the corresponding ferrous ion reaction. This again could be interpreted on Zwolinski, Marcus, and Eyring's picture as due to the smaller amount of reorganisation required by the complex ion in the transition state.

FIG. 1.

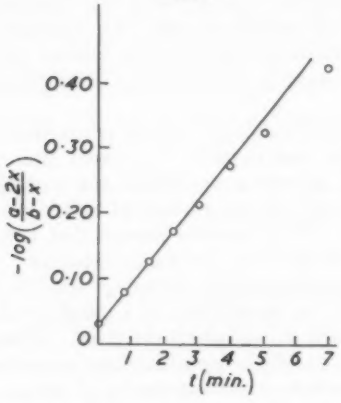
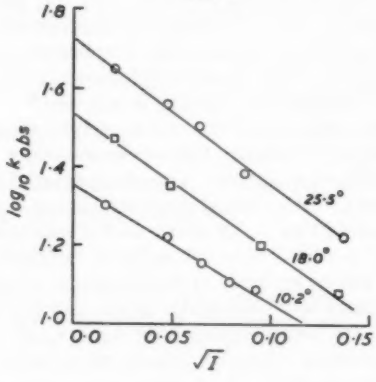


FIG. 2.



The Effect of Hydrogen-ion Concentration on the Rate of Reaction.—At very low ionic strength there was no detectable effect of hydrogen-ion concentration on the rate but at ionic strengths greater than about 0·05 the rate increased with it. The effect was more pronounced the higher the ionic strength. Table 1 shows the results of experiments

TABLE 1. *The effect of hydrogen ions on the rate of the reaction at* 25·5°.

I	—	—	1·76	—	—	0·106	—
$[H^+]$ (M)	1·76	1·06	0·35	0·00	0·106	0·070	0·00
k_{obs} (l. mole^{-1} sec.$^{-1}$)	3·13	2·50	1·96	1·70	7·78	7·54	7·10

carried out at $I = 0{\cdot}106$ and $I = 1{\cdot}76$. A plot of k_{obs} against $[\overline{H}^+]$ in each case is linear; this can be explained by assuming either that $S_2O_8^{2-}$ reacts both with $Os(dipy)_3^{2+}$ and its conjugate acid $HOs(dipy)_3^{3+}$, or that $Os(dipy)_3^{2+}$ reacts both with $S_2O_8^{2-}$ and its conjugate acid $HS_2O_8^-$. In either case one obtains the following expression:

$$k_{obs} = (k_a[H^+] + k_bK_a)/(K_a + [H^+]) \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where k_a and k_b are the velocity constants for the reactions involving the conjugate acid and base species respectively, and K_a is the dissociation constant of the acid.

If $K_a \gg [H^+]$, then expression (4) reduces to

$$k_{obs} = k_a[H^+]/K_a + k_b \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

and a plot of k_{obs} against $[H^+]$ is linear with slope equal to k_a/K_a and intercept k_b. Values of k_a/K_a (sec.$^{-1}$/mole^2) at 25·5° at different ionic strengths (in parentheses) were 0·80 (1·76), 2·38 (0·53), 6·40 (0·106), and $13{\cdot}0 \pm 3{\cdot}0$ (0·035). The increase as the ionic strength

[9] Gladstone, Laidler, and Eyring, "Theory of rate processes," McGraw-Hill, New York, 1941.

XUM

decreases is consistent with either of the mechanisms above since in either case k_a/K_a, in the Debye–Hückel region at any rate, is given by the expression

$$\log (k_a/K_a) = \text{constant} - 4{\cdot}0\sqrt{I} \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

It is noteworthy that Kolthoff and Miller [10] postulated the existence of the acid $HS_2O_8^-$ in order to account for the dependence on the hydrogen-ion concentration of the rate of decomposition of $S_2O_8^{2-}$, and estimated the value of its dissociation constant to be 1·0 or greater at $I = 0{\cdot}01$. These experiments show that at $I = 0{\cdot}106$, K_a must be about 1·0 or greater in order to account for the linearity of k_{obs} with $[H^+]$. This order of magnitude of K_a is therefore not inconsistent with participation of the species $HS_2O_8^-$ in the reaction.

The absence of any detectable effect of $[H^+]$ at low ionic strength is presumably due to the fact that under such conditions $k_b \gg k_a[H^+]/K_a$ so that changes in k_{obs} are small, and lie within experimental error.

The Effect of Nitrate, Chloride, and Sulphate Ions.—The rate of the reaction was the same, within experimental error, whether nitrate or perchlorate ions were used to adjust ionic strength. Thus at $I = 0{\cdot}85$ and $I = 0{\cdot}53$ values of k_{obs} with nitrate ion were 2·39 l. mole^{-1} sec.$^{-1}$ and 3·11 l. mole^{-1} sec.$^{-1}$ respectively. The corresponding values with perchlorate ion were 2·24 and 3·12 l. mole^{-1} sec.$^{-1}$. On the other hand, at $I = 0{\cdot}85$ the value of k_{obs} obtained with chloride ion was 4·00 l. mole^{-1} sec.$^{-1}$ and with sulphate 5·78 l. mole^{-1} sec.$^{-1}$. At constant ionic strength k_{obs} increased as the concentration of chloride or sulphate ions increased as shown in Table 2. In each case a plot of k_{obs} against anion

TABLE 2. *The effect of chloride and sulphate ions on* k_{obs} (*l. mole*$^{-1}$ *sec.*$^{-1}$) *at* $I = 0{\cdot}10$ *and* 25·5°.

$[Cl^-]$ (M) ...	0·10	0·07	0·04	0·00	$[SO_4^{2-}]$ (M)...	0·033	0·022	0·011	0·00
k_{obs}	9·45	8·59	8·10	7·10	k_{obs}	10·9	9·64	8·10	7·10

concentration is linear. One interpretation of this is that both chloride and sulphate anions form ion-pair complexes with $Os(dipy)_3^{2+}$ which also react with $S_2O_8^{2-}$. If, for example, in the case of chloride it is assumed that an ion-pair complex $[Os(dipy)_3Cl]^+$ as well as $Os(dipy)_3^{2+}$ reacts with $S_2O_8^{2-}$, then

$$k_{obs} = (k_1[Cl^-] + k_2K_{Cl})/(K_{Cl} + [Cl^-]) \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

where k_1 and k_2 are the velocity constants for the reactions involving $[Os(dipy)_3Cl]^+$ and $Os(dipy)_3^{2+}$ respectively, and K_{Cl} is the dissociation constant of $[Os(dipy)_3Cl]^+$. If $K_{Cl} \gg [Cl^-]$, eqn. (7) approximates to

$$k_{obs} = k_1[Cl^-]/K_{Cl} + k_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

and a plot of k_{obs} against $[Cl^-]$ is linear. At very high ionic strength the plot of k_{obs} against $[Cl^-]$ was no longer linear; at $I = 0{\cdot}85$ k_{obs} (l. mole^{-1} sec.$^{-1}$) was 4·00, 3·25, 2·79, 2·41, and 2·24 at $[Cl]^- = 0{\cdot}85$, 0·60, 0·40, 0·20, and 0·00M respectively, showing that k_{obs} is proportional to $[Cl^-]^x$, where $1 < x < 2$. A possible explanation is that at high chloride concentration other ion-pair chloro-complexes, *e.g.*, $[Os(dipy)_3Cl_2]^0$, also take part in the reaction. At very low ionic strength there was no noticeable effect of chloride ions on the rate of the reaction, but presumably, as with hydrogen ions, changes in k_{obs} were so small as to be within experimental error.

Much the same behaviour was observed with sulphate ions. At $I = 0{\cdot}90$, k_{obs} was almost proportional to the square of the sulphate ion concentration whereas at very low ionic strength k_{obs} was very much the same as in the presence of perchlorate ions.

Although no spectrophotometric evidence was obtained for the formation of ion-pair complexes between $Os(dipy)_3^{2+}$ and chloride or sulphate ions, there is some justification for assuming their existence since other complex ions are known to form such complexes. Thus

[10] Kolthoff and Miller, *J. Amer. Chem. Soc.*, 1951, **73**, 3055.

XUM

$Co(NH_3)_6^{3+}$ forms mono-complexes with chloride and sulphate ions having association constants of 4·1 and 3×10^3 moles^{-1} at 25° and $I = 0{\cdot}05$ and 0·0 respectively.[11,12] Association of sulphate ions has also been shown to occur with $[Co(NH_3)_5\ H_2O]^{3+}$,[12] the association constant of the monosulphate complex being about 16·0 moles^{-1} at 31·1° and $I = 1{\cdot}0$. These results indicate that for the same charge sulphate is more firmly bound than chloride.

Although absolute values of the association constants for the chloride and sulphate complexes of $Os(dipy)_3^{2+}$ cannot be obtained from the results of these experiments, some idea of the relative strength of attachment of these ions can be deduced from the slopes of the plots of k_{obs} against anion concentration. These slopes give values of k_1/K_{anion}. At $I = 0{\cdot}10$ the values are 7·7 and 120·0 sec.$^{-1}$/mole^2 for chloride and sulphate respectively. It seems reasonable to assume that the less positively charged sulphate complex would not react faster with $S_2O_8^{2-}$ than the chloride complex, and hence that the higher value of k_1/K_{anion} for sulphate arises through a smaller value of K_{anion}. This in turn implies a higher value for the association constant of the sulphate complex, which is in accord with the observations on other systems.

Experimental

Materials.—Solutions. Trisdipyridylosmium(II) perchlorate was prepared and standardised as previously.[3]

" AnalaR " potassium peroxydisulphate was used after being dried at 105°. A stock solution was made by weight and stored at 0° in a dark bottle. Fresh solutions were prepared after every four or five days.

Sodium perchlorate solution was prepared by neutralising " AnalaR " perchloric acid with " AnalaR " sodium hydroxide and filtering.

B.D.H. 60% " AnalaR " perchloric acid was used for the experiments involving hydrogen ions. All other reagents were of " AnalaR " quality.

Conductivity water was used for all solutions, obtained as previously.[3]

Procedure.—The reaction was followed spectrophotometrically as previously.[3] Duplicate kinetic runs agreed to within 3%.

University College, Ibadan, Nigeria. [*Received, January 1st,* 1958.]

[11] Garrick, *Trans. Faraday Soc.*, 1937, **33**, 486.
[12] Taube and Posey, *J. Amer. Chem. Soc.*, 1953, **75**, 1463.

---

442. *Higher Complex Fluorides of Tungsten.*

By G. B. Hargreaves and R. D. Peacock.

Work on the complex fluorides of tungsten has been continued; the salts K_2WF_8, K_3WF_8, $RbWF_7$, $CsWF_7$, and $CsWOF_5$ have been obtained and characterised.

Work with elementary fluorine and molybdenum carbonyl [1] yielded two lower fluorides of molybdenum, the pentafluoride MoF_5 and the tetrafluoride MoF_4. Starting from a parallel investigation with tungsten carbonyl, we have found several compounds in which tungsten apparently exhibits a high co-ordination number with respect to fluorine.

Ruff found that molybdenum and tungsten hexafluorides are absorbed by the alkali fluorides, and Cox, Sharp, and Sharpe [2] obtained definite compounds of the general formulæ M_2MoF_8 and M_2WF_8, although, as Clark and Emeléus [3] showed that dry alkali fluorides do not absorb the hexafluorides we reopened the subject. We now report the preparation of complex fluorides of sexivalent tungsten; these are K_2WF_8, $RbWF_7$, and $CsWF_7$.

[1] Peacock, *Proc. Chem. Soc.*, 1957, 59.
[2] Cox, Sharp, and Sharpe, *J.*, 1956, 1242.
[3] Clark and Emeléus, *J.*, 1957, 4778.

In addition, $CsWOF_5$ and K_3WF_8 were characterised. We believe we have also solved some earlier problems.

Experimental

Attempted Preparation of Lower Tungsten Fluorides.—(*a*) Fluorine diluted with nitrogen was allowed to interact with resublimed tungsten carbonyl under conditions similar to those described for molybdenum carbonyl.[1] There is no action below 0°; above this temperature intermittent combination takes place and tungsten hexafluoride WF_6 and carbonyl fluoride COF_2 are formed: $W(CO)_6 + 9F_2 \longrightarrow WF_6 + 6COF_2$.

(*b*) Iodine pentafluoride, prepared from the elements and purified by trap-to-trap distillation in a vacuum, was condensed on tungsten carbonyl. Iodine was liberated, carbon monoxide was evolved, and the presence of tungsten hexafluoride was inferred from its physical properties. All the products were easily volatile, and no lower fluorides were found:

$$5W(CO)_6 + 6IF_5 \longrightarrow 5WF_6 + 30CO + 3I_2.$$

Complex Fluorides of Tungsten.—Tungsten carbonyl was sublimed in a high vacuum. Tungsten hexafluoride and iodine pentafluoride were prepared from the elements and sublimed or distilled in a vacuum. The alkali iodides and fluorides were carefully dried, the former at 100° and the latter by heating them to incipient fusion.

(1) *Reaction of Tungsten Carbonyl and Alkali Iodide with Iodine Pentafluoride.*—(a) *Mixture* $W(CO)_6 : KI = 1 : 1$. Warmed together, these produced *dipotassium octafluorotungstate*(VI) K_2WF_8, a white solid readily freed from iodine and excess of iodine pentafluoride by heating it in a vacuum at 150° for 30 min. (Found: W, 44·1; F, 36·3%; equiv., 415. K_2WF_8 requires W, 44·4; F, 36·7%; equiv., 415): $5W(CO)_6 + 10KI + 8IF_5 = 5K_2WF_8 + 9I_2 + 30CO$. It is stable in dry air but decomposes in a moist atmosphere with rapid attack on glass containers. It is completely and easily soluble in water to a solution which smells of hydrofluoric acid. Debye *X*-ray photographs, detailed below, show a cubic unit cell with $a = 10{\cdot}03$ Å.

(b) *Mixture* $W(CO)_6 : CsI = 1 : 1$. Although the white solid from this reaction had similar properties to the above potassium salt, and a composition near to the formula Cs_2WF_8, Debye *X*-ray photographs disclosed a phase isostructural with that [4] of $CsWF_6$ indicating the probable presence of the oxyfluoride $CsWOF_5$ (see below) (Found: W, 30·7; F, 26·9%. Calc. for Cs_2WF_8: W, 30·6; F, 25·3%. Calc. for a mixture of $CsWOF_5 : Cs_2SiF_6 = 2 : 1$: W, 29·1; F, 24·1%).

(c) *Mixture* $W(CO)_6 : NaI = 1 : 1$. Under rigorously dry conditions tungsten was not found in the product, a result in conformity with the behaviour of tungsten hexafluoride described below. It is difficult to dry sodium iodide thoroughly without slight oxidation or hydrolysis, so products were sometimes obtained with a composition approximately Na_2WF_8, but the Debye *X*-ray photographs showed a phase isostructural with that of $NaWF_6$, which was most probably the oxyfluoride $NaWOF_5$ (Found: W, 49·3; F, 38·1. Calc. for Na_2WF_8: W, 48·2; F, 39·8%. Calc. for a mixture $NaWOF_5 : Na_2SiF_6 = 2 : 1$: W, 44·6; F, 36·9%.

(d) *Mixture* $W(CO)_6 : KI = 2 : 1$. Treatment of this mixture with iodine pentafluoride yielded a white solid which could be freed from iodine and iodine pentafluoride by heating it in a vacuum at 150° for 30 min. This was *tripotassium octafluorotungstate*(V) (Found: W, 40·9; F, 38·9%; equiv., 431. K_3WF_8 requires W, 40·6; F, 40·1%; equiv., 453), which is stable in dry air but decomposed by moist air. Its aqueous solution is pale green, unlike the blue or purple solution of potassium hexafluorotungstate(V) KWF_6. Debye *X*-ray photographs show a rhombohedral unit cell with $a = 9{\cdot}75$ Å and $\alpha = 86{\cdot}4°$. (Molybdenum appears to form a similar compound which is still under investigation.)

(e) *Mixture* $W(CO)_6 : NaI = 2 : 1$. Again quinquevalent tungsten was produced, but Debye *X*-ray photographs showed the product to be a mixture containing $NaWF_6$. The material dissolved in water to give the blue colour characteristic of the WF_6^- ion.

(2) *Reaction of Tungsten Hexafluoride and Alkali Fluoride.*—(a) *In absence of solvent.* On rigorously dried material our results agree with those of Clarke and Emeléus, who found there was no combination. With slightly moist potassium fluoride, however, there was rapid reaction in the cold; the impure product contained HF and was not amenable to *X*-ray examination in glass. It had a composition near to K_2WF_8 (Found: W, 39·0; F, 35·3%). Cæsium fluoride, also slightly moist, gave a product containing 24·1% of tungsten; according to the Debye *X*-ray photographs it contained $CsWOF_5$.

XUM

(b) *In the presence of iodine pentafluoride.* With dry potassium fluoride dipotassium octafluorotungstate K_2WF_8 was formed (Found: W, 44·4; F, 36·8%), a conclusion supported by Debye *X*-ray photographs. So far we have been unable to dry either rubidium or cæsium fluorides to give a stoicheiometric product. The moist salts yielded complex oxyfluorides, isostructural with $RbWF_6$ and $CsWF_6$, of which the *cæsium oxypentafluorotungstate*(VI), a white solid stable in dry air, was analysed (Found: W, 43·2; F, 23·1%. $CsWOF_5$ requires Cs, 42·0; F, 21·7%). Our preparation attacked glass slowly; we ascribe this to HF or moisture and do not believe it is characteristic of the pure compound. The salt dissolves in water to a colourless solution.

(3) *Reaction of Tungsten Hexafluoride and Alkali Iodide in the Presence of Iodine Pentafluoride.*—Alkali iodides were used because, except for lithium and sodium iodides, they are more easily purified and dried than the fluorides. With potassium iodide, dipotassium octafluorotungstate was formed (Found: W, 44·3; F, 36·6%). Debye *X*-ray photographs supported the conclusion reached from the analysis. Neither rubidium nor cæsium iodides gave a product corresponding in composition to that from potassium iodide, but gave *rubidium heptafluorotungstate*(VI) and *cæsium heptafluorotungstate*(VI) (Found: W, 45·3; F, 33·4%; equiv., 389. $RbWF_7$ requires W, 45·7; F, 33·1%; equiv., 402. Found: W, 40·0; F, 29·5%; equiv., 460. $CsWF_7$ requires W, 40·0; F, 28·9%; equiv., 460). Both heptafluorotungstates resemble K_2WF_8 in appearance and properties: $5WF_6 + 5RbI + IF_5 \longrightarrow 5RbWF_7 + 3I_2$; $5WF_6 + 5CsI + IF_5 \longrightarrow 5CsWF_7 + 3I_2$. Debye *X*-ray photographs, detailed below, show $CsWF_7$ to have a cubic unit cell with $a = 5{\cdot}49$ Å. The three fluoro-complexes of sexivalent

TABLE 1.

		K_2WF_8			$RbWF_7$		
N	Indices	Intensity	$\sin^2\theta \times 10^4$ found	$\sin^2\theta \times 10^4$ calc.	Intensity	$\sin^2\theta \times 10^4$ found	$\sin^2\theta \times 10^4$ calc.
4	200	s	332	318	s	312	304
5	210	w	414	397	ms	393	380
8	220	vs	671	635	vs	621	608
9	300 221	vw	727	714	ms	698	684
10	310	vvw	829	794	—	—	—
12	222	vw	969	953	vw	923	911
13	320	vvw	1055	1032	vw	1006	987
14	321	vw	1135	1112	vw	1068	1063
16	400	ms	1296	1270	ms	1227	1215
17	410 322	w	1373	1350	vw	1302	1291
20	420	w	1617	1588	—	—	—
21	421	s	1690	1667	ms	1609	1595
24	422	vs	1928	1906	vs	1840	1823
25	430 500	w	1988	1985	vw	1918	1899
26	511 431	vw	2085	2064	vw	1994	1975
29	520 432	ms	2325	2303	w	2222	2203
30	521	vw	2409	2382	vw	2292	2279
32	440	w	2566	2541	w	2445	2430
33	522 441	w	2648	2620	vw	2525	2506
36	600 442	w	2877	2858	vw	2755	2734
37	610	w	2963	2938	vw	2829	2810
40	620	ms	3203	3176	ms	3052	3038
41	443 621 540	vs	3281	3255	ms	3130	3114
42	541	w	3369	3335	vw	3215	3190
45	630 542	w	3601	3573	w	3433	3418
46	631	vw	3683	3652	vw	3514	3494
48	444	—	—	—	vw	3658	3646
49	700 632	w	3917	3891	w	3745	3722

XUM

TABLE 1. (*Continued.*)

		K_2WF_8			$RbWF_7$		
N	Indices	Intensity	$\sin^2\theta \times 10^4$ found	$\sin^2\theta \times 10^4$ calc.	Intensity	$\sin^2\theta \times 10^4$ found	$\sin^2\theta \times 10^4$ calc.
50	543 710 550	vw	4015	3970	vvw	3814	3798
53	720 641	w	4235	4208	w	4065	4025
54	552 721 633	vw	4320	4288	vw	4134	4101
56	642	ms	4465	4446	s	4275	4253
61	650 643	w	4862	4843	vw	4641	4633
62	732 651	w	4955	4923	vw	4735	4709
65	810 740	ms	5183	5160	w	4948	4937
66	811 741	w	5281	5240	vw	5050	5013
69	821 742	ms	5499	5479	w	5259	5241
70	653	vw	5586	5558	vw	5338	5317
73	830 661	w	5817	5796	—	—	—
74	743 831 750	vw	5908	5875	—	—	—
77	832 654	ms	6142	6114	w	5861	5848
81	744 900 663 841	ms	7456	6431	vw	6193	6152
84	842	—	—	—	w	6380	6380
86	655 921 761	ms	6859	6828	—	—	—
89	843 922 762 850	w	7084	7067	—	—	—
90	754 930 851	ms	7168	7146	—	—	—
93	852	vvw	7403	7384	—	—	—
94	932 763	vw	7485	7464	—	—	—
98	770 941 853	w	7794	7781	—	—	—
101	10·10 861 942 764	s	8041	8019	w	7674	7670
105	10·21 854	s	8357	8337	—	—	—
109	10·30 863	ms	8664	8654	—	—	—
110	10·31 952 765	ms	8735	8734	—	—	—
113	10·32 944 870	ms	8968	8972	—	—	—
115	953	ms	9096	9131			
117	10·41 960 872	ms	9296 9315	9290	vw	8810	8810

		$CsWF_7$					$CsWF_7$		
N	Indices	Intensity	$\sin^2\theta \times 10^4$ found	$\sin^2\theta \times 10^4$ calc.	*N*	Indices	Intensity	$\sin^2\theta \times 10^4$ found	$\sin^2\theta \times 10^4$ calc.
1	100	w	279	273	18	411 330	w	4932	4910
2	110	vs	559	546	20	420	vw	5486	5456
4	200	w	1105	1091	22	332	vvw	6027	6002
6	211	s	1654	1637	26	431 500	w	7108	7093
8	220	w	2205	2182					
10	310	ms	2758	2728					
12	222	vw	3306	3274	30	521	vw	8209	8184
14	321	s	3846	3819	34	530	vvw	9276	9275
16	400	vvw	4393	4365					

tungsten, and the complex oxyfluoride, are all slightly paramagnetic (μ_{eff} ~0·2 B.M.) at room temperature.

Analysis.—Tungsten. The complexes were dissolved in water (quinquevalent tungsten if present was oxidised with nitric acid) and the tungsten was precipitated by the cinchonine–tannin method and weighed as WO_3 after ignition of the precipitate at 800°.

Fluorine. The compound was broken down with sulphuric acid and fluorine determined in the fluorosilicic acid distillate by precipitation as lead chlorofluoride PbClF and estimation of the chloride equivalent by the Volhard method.

X-Ray Photography.—Since the compounds were too hygroscopic for transference in a dry-box, the thin-walled Pyrex capillary of about 0·5 mm. diameter was sealed to the preparation line. The compound was powdered by shaking it with a number of glass beads, and was then shaken into the capillary. A 9-cm. camera and Co-$K\alpha$ radiation in conjunction with an iron filter were used. A 19-cm. camera gave no better photographs. For results, see Table 1.

Densities.—Carbon tetrachloride was carefully dried by distillation over phosphoric oxide. A 2 ml. density bottle with a stopper was used. About 1 g. of material was required for each determination. The results are presented in Table 2.

Discussion

The results show the necessity of thoroughly drying the reactants and emphasise the diagnostic value of *X*-ray photography. The earlier failure to prepare complex rubidium and cæsium fluorotungstates(VI) from the carbonyl reaction may well be due to the difficulty of freeing iodine pentafluoride from HF and SiF_4. Complex oxyfluorides are clearly formed preferentially with even small quantities of moisture or hydrogen fluoride present, except perhaps when the alkali metal is potassium.

If sufficient alkali iodide is present when tungsten carbonyl interacts with iodine pentafluoride, quinquevalent complex fluorides are formed. We do not know why this is so, but only suggest that with large amounts of free iodine the increase in " basicity " is sufficient to stabilise W^{5+} in iodine pentafluoride. It is noteworthy that whereas sodium iodide gives a hexafluorotungstate(v) under these conditions,[cf. 4] potassium iodide gives an octafluorotungstate(v) K_3WF_8.

Sexivalent complex fluorides of tungsten are best prepared by the addition of excess of tungsten hexafluoride to alkali iodide in presence of iodine pentafluoride. We agree with Clark and Emeléus that rigorously dried alkali-metal fluorides do not combine appreciably with tungsten hexafluoride and our work also indicates that a solvent such as iodine pentafluoride is necessary to promote the reaction.

Table 2.

	Unit cell size (Å)	Density (g./ml.)	Formula units per unit cell	Density calc. from unit cell (g./ml.)
K_2WF_8	$a_0 = 10{\cdot}03$ (Cubic)	4·10	6	4·09
$RbWF_7$	$a_0 = 10{\cdot}27$,,	4·14	(6·76)	(4·14)
$CsWF_7$	$a_0 = 5{\cdot}49$,,	4·54	1	4·61
$NaWOF_5$	$a_0 = 8{\cdot}17$,,	—	—	—
$CsWOF_5$	$a_0 = 5{\cdot}31$; $\alpha = 95{\cdot}5°$ (Rhombohedral)	—	—	—
K_2WF_8	$a_0 = 9{\cdot}75$; $\alpha = 86{\cdot}4°$,,	—	—	—

Debye *X*-ray photographs show that the three sexivalent complex fluorides have simple cubic symmetry, but that whereas K_2WF_8 and $RbWF_7$ seem to be closely related in structure $CsWF_7$ stands by itself. Density measurements indicate that the unit cell of K_2WF_8 contains 6 formula units, and that of $RbWF_7$ about 6·8 formula units (Table 2). In each case, therefore, the unit cell probably contains 48 fluorine atoms. Without a complete set of intensity measurements we cannot be specific about their structures, but it is reasonable to imagine the 48 fluorine atoms to be divided into 8 octahedrally arranged sets of 6 with statistical distributions of tungsten and alkali-metal atoms between them. $CsWF_7$ contains only one formula unit in the unit cell and the absent reflections suggest

[4] Hargreaves and Peacock, *J.*, 1957, 4212.

XUM

a cæsium chloride arrangement of cæsium and tungsten atoms; nothing can be said about the positions of the fluorine atoms. Since the structures of the salts depend markedly on the size of the alkali-metal atom, the absence of a stable sodium fluorotungstate(VI) is scarcely surprising.

The chief interest in the complex sexivalent fluorotungstates lies in the covalency of the tungsten atom. Octacovalent tungsten is well known in the quadrivalent octacyanotungstates $M_4W(CN)_8$ and osmium, which lies in the same period of the Periodic Table, forms an octafluoride OsF_8. Whether tungsten has a covalency greater than six in our compounds is uncertain, although in the cæsium salt a covalency of seven seems likely.

We thank Professor G. Wilkinson for his encouragement, Mining and Chemical Products Limited for a gift of cæsium salts, Imperial Chemical Industries Limited, General Chemicals Division, for the use of a fluorine cell, and the Department of Scientific and Industrial Research for a maintenance grant (to G. B. H.).

IMPERIAL COLLEGE, LONDON, S.W.7. [*Received, February 14th*, 1958.]

---

443. *Chemical Action of Ionising Radiations in Solution. Part XXI.* The Action of ^{60}Co γ-Radiation on Aqueous Solutions of Ethylene at Different Pressures.*

By P. G. CLAY, G. R. A. JOHNSON, and J. WEISS.

^{60}Co γ-Irradiation of water saturated with ethylene (1 atm.), in the absence of oxygen, yields aldehydes, mainly acetaldehyde and *n*-butyraldehyde, and hydrogen peroxide, together with an oily polymer. From water, saturated with different ethylene–oxygen mixtures, the irradiation products are: acetaldehyde, formaldehyde, glycollaldehyde, hydrogen peroxide, and relatively small amounts of an organic hydroperoxide. Their formation at different ratios of [ethylene]/[oxygen], at different pH values, and in the presence of added ferrous salt has been studied. Irradiations of aqueous ethylene–oxygen solutions at higher pressures (up to 10 atm.) showed that the products and their yields, under these conditions, are not markedly different from those at lower pressures. This finding is contrary to that of Henley *et al.*[1,2]

RECENT investigations have provided much information about the reactions of various functional groups when compounds in aqueous solution are subjected to the action of ionising radiations.[3] Little attention has been paid, however, to the reactions occurring when solutions of unsaturated compounds are irradiated in the presence of molecular oxygen, except for the polymerisation of certain vinyl compounds, which occurs on irradiation of their solutions in the absence of oxygen.[cf. 3] We have now studied the action of ^{60}Co γ-rays on aqueous solutions of ethylene as part of an investigation into the effects of ionising radiations on simple unsaturated compounds.

RESULTS

Irradiations in the Absence of Oxygen.—Irradiation of ethylene-saturated water in absence of oxygen yielded an oily polymer and a mixture of aldehydes, in which acetaldehyde and *n*-butyraldehyde were identified by paper chromatography of their 2 : 4-dinitrophenylhydrazones. Some spots with R_F values greater than those of acetaldehyde and butyraldehyde

* Part XX, *J.*, 1957, 1358.

[1] Henley and Schwartz, *J. Amer. Chem. Soc.*, 1955, **77**, 3167.
[2] Henley, Schiffries, and Barr, *Ass. Inst. Chem. Eng. J.*, 1956, **2**, 211.
[3] Collinson and Swallow, *Chem. Rev.*, 1956, **56**, 471.

XUM

were also observed, indicating that other longer-chain aldehydes were present, but these have not been identified. Hydrogen peroxide was also formed. The yields of total aldehyde and hydrogen peroxide were linear with radiation dose up to the highest doses used [$\sim 12 \times 10^{-6}$(ev/N) ml.$^{-1}$] having the values: $G(H_2O_2) = 0{\cdot}40 \pm 0{\cdot}10$ and G(total aldehyde) = $0{\cdot}24 \pm 0{\cdot}05$ at pH 1·2; and $G(H_2O_2) = 0{\cdot}28 \pm 0{\cdot}10$ and G(total aldehyde) = $0{\cdot}090 \pm 0{\cdot}030$ at pH 5·0 (where G = number of molecules formed per 100 ev of radiation-energy absorbed).

TABLE 1. *Irradiation of aqueous solutions of ethylene–oxygen mixtures at* pH 1·2.

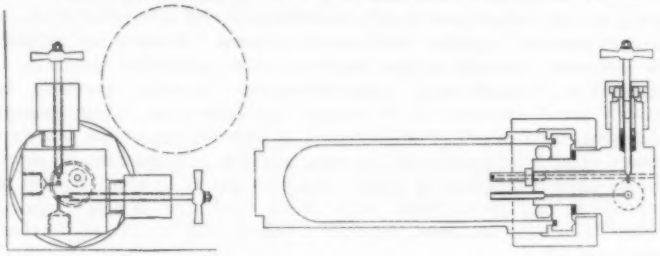
Dependence of initial yields on the [ethylene]/[oxygen] ratio in the gaseous phase (total pressure, 1 atm.). Dose rate: 1×10^{-7} (ev/N) ml.$^{-1}$ min.$^{-1}$.

	G values (molecules formed per 100 ev)			
Ratio $[C_2H_4]/[O_2]$	(H·CHO + CH_3·CHO)	CH_3(OH)·CHO	H_2O_2	R·O·OH
0·11	1·7	1·8	2·8	0·6
1·00	2·4	2·4	2·4	0·4
3·00	3·0	2·5	2·6	0·4
9·00	3·0	2·4	2·4	0·3

Some experiments were carried out in the presence of ferric ammonium sulphate, formation of ferrous ion being determined by complex-formation with *o*-phenanthroline and measurement of the absorption at 510 mμ. At a concentration of 5×10^{-2}M-ferric ion $G(Fe^{2+}) = 6{\cdot}0$ and G(total aldehyde) = 0·70; at 10^{-3}M-ferric ion $G(Fe^{2+}) = 1{\cdot}0$ and G(total aldehyde) = 0·70.

Irradiations in Presence of Oxygen.—The products detected in irradiated ethylene–oxygen solutions were acetaldehyde, formaldehyde, glycollaldehyde and hydrogen peroxide. An unidentified organic peroxide was also detected in low yields ($G \simeq 0{\cdot}4$).

FIG. 1. *Steel bomb used for irradiation of solutions of oxygen–ethylene mixtures under pressure.*



As preliminary quantitative experiments showed that the yields of the products depended, to some extent, upon the relative concentrations of ethylene and oxygen in solution we studied the effect of the ratio [ethylene]/[oxygen] on the yields. Table 1 gives the initial yields (G values) of the products at values of this ratio ranging from 0·11 to 9·0; over this range, the yields are relatively insensitive to changes in the ethylene concentration. For the quantitative experiments, therefore, a gas mixture of [ethylene]/[oxygen] = 3·0 was used, corresponding to solution concentrations of ethylene and oxygen of 3×10^{-3}M and 3×10^{-4}M, respectively, as calculated from the known solubilities of these gases at 19°. Also, the concentration of ethylene was determined bromometrically and that of oxygen by polarography; the values obtained were in good agreement with the above calculated values.

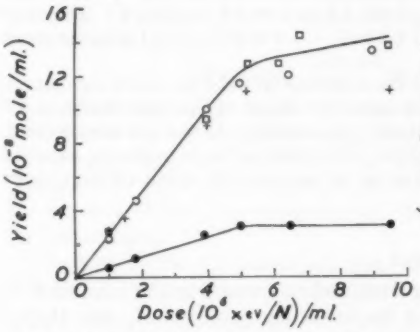
In view of a report [1,2] that high yields of acetaldehyde ($G \simeq 60$) were obtained when solutions of ethylene–oxygen were irradiated at pressures above 8 atm., solutions of a 1 : 1 mixture at a total pressure of 10 atm. have been investigated. The yields of the products obtained were: $G(H_2O_2) = 2{\cdot}6$, G(acetaldehyde + formaldehyde) = 1·3, and G(glycollaldehyde) = 1·5. This confirms the results obtained on varying the ratio ([ethylene]/[oxygen]), and that, contrary to the findings of Henley *et al.*,[1,2] this increase in the ethylene concentration does not lead to a chain reaction and has, indeed, very little effect on the yield of the products.

The yields were determined as a function of total radiation dose at pH 1·2 (Fig. 2), 2·5, 3·2, 5·5 (Fig. 3), and 7·5. At all these values the yield–dose curves were initially linear but eventually showed a relatively sharp decrease in the yield per unit dose, attributable to the utilisation, by

XUM

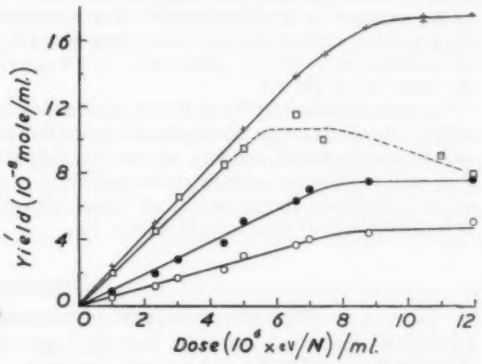
the radiation-induced reactions, of all the oxygen originally present in solution. Diffusion of oxygen into the solution is relatively slow, and when practically all the original oxygen has

FIG. 2. *Irradiation of aqueous solutions of ethylene–oxygen mixtures* (3 : 1 *in the gaseous phase; total pressure* 1 *atm.*) *with* ^{60}Co *γ-rays.*



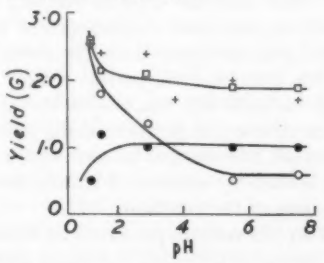
Dependence of yield of hydrogen peroxide (□), glycollaldehyde (+), acetaldehyde (○), and formaldehyde (●) on total radiation dose at pH 1·2.

FIG. 3. *Irradiation of aqueous solutions of ethylene–oxygen mixtures* (3 : 1 *in the gaseous phase; total pressure* 1 *atm.*) *with* ^{60}Co *γ-rays.*



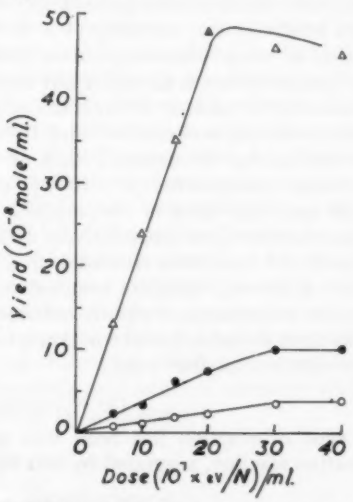
Dependence of yield of hydrogen peroxide (□), glycollaldehyde (+), acetaldehyde (○), and formaldehyde (●) on total radiation dose at pH 5·5.

FIG. 4. *Irradiation of aqueous solutions of ethylene–oxygen mixtures* (3 : 1 *in the gaseous phase; total pressure* 1 *atm.*) *with* ^{60}Co *γ-rays.*



pH-Dependence of the initial yields of hydrogen peroxide (□), glycollaldehyde (+), acetaldehyde (○), and formaldehyde (●).

FIG. 5. *Irradiation of aqueous solutions of ethylene–oxygen mixtures* (3 : 1 *in the gaseous phase; total pressure* 1 *atm.*) *containing ferrous sulphate* (10^{-3}M) *at* pH 1·2.



Yield–dose dependence of the products: ferric ion (△), acetaldehyde (○), and formaldehyde (●).

been used the irradiation proceeds virtually in the absence of oxygen. The results (Fig. 2) therefore indicate that all the oxygen originally present in solution is used up, at pH 1·2, after a dose of about 5×10^{-6}(ev/*N*) ml.$^{-1}$. Since the initial oxygen concentration is 3×10^{-4}M,

this gives a value for the rate of oxygen utilisation $G(O_2) \simeq 6{\cdot}0$. Similarly, at pH 5·5 $G(O_2) \simeq 4{\cdot}0$.

The pH-dependence of the initial G-values for the formation of the different products is shown in Fig. 4; each value was taken from a yield–dose plot. At pH 1·2, the major products are acetaldehyde and glycollaldehyde, in almost equal amounts; as the pH is increased, the yield of these products decreases and the yield of formaldehyde increases. At pH 5·5 the major product is glycollaldehyde; less acetaldehyde and formaldehyde are formed. The total yield of organic products falls from $G \simeq 5{\cdot}9$ at pH 1·2 to $G \simeq 3{\cdot}6$ at pH 5·5. The yield of hydrogen peroxide also falls from $G = 2{\cdot}6$ at pH 1·2 to $G = 1{\cdot}9$ at pH 5·5 and remains about the same up to pH 7·5.

Ferrous sulphate (10^{-3} and 10^{-2}M) when added to the solutions (at pH 1·2), before irradiation, altered the yields of acetaldehyde and formaldehyde from the values of G(acetaldehyde) = 2·5 and G(formaldehyde) = 0·5 to 1·2 and 3·8, respectively; glycollaldehyde was not then formed. The yield of ferric ion corresponded to $G(Fe^{3+}) = 23{\cdot}0$. The yields of these products, obtained in the presence of ferrous salt, were linear with dose up to the point at which all the oxygen in the solution had been consumed (Fig. 5).

Discussion

The net result of the absorption of ionising radiations by water is the formation of hydrogen atoms and hydroxyl radicals [5] and of the molecular products H_2 and H_2O_2.[6] The yields are related by the stoicheiometry:

$$2G^{w}(H_2) + G^{w}(H) = 2G^{w}(H_2O_2) + G^{w}(OH) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where the coefficients $G^{w}(X)$ refer to the yields in molecules of X per 100 ev of radiation energy absorbed by the water. There is no general agreement on the exact values of these coefficients and they probably depend on the pH of the irradiated solution and on the concentration and chemical nature of any solute present. For the present discussion, values of $G^{w}(H_2O_2) = 0{\cdot}8$, $G^{w}(OH) = 2{\cdot}7$, and $G^{w}(H) = 3{\cdot}8$ will be assumed.[7,8]

Ethylene has disadvantages as a solute in radiation studies. It is inconvenient to handle, and its relatively low solubility (4×10^{-3}M at 1 atm. and 15°) makes it difficult to study the effect of solute concentration on yield. The latter disadvantage is serious, since the solute concentration is an important factor in determining the processes occurring during irradiation of a solution of organic compounds.[9] The ethylene–oxygen system, studied at concentrations between 10^{-4} and 10^{-2}M-ethylene, showed little dependence of yield on concentration, so we assumed that at the solute concentration used for most of the quantitative experiments (3×10^{-3}M), attack on the ethylene will be due mainly to free radicals and that most of the available hydroxyl radicals will react with the ethylene. Oxygen concentration has relatively little influence on the yields, these being linear with dose under all conditions studied until all, or nearly all, the oxygen present has been consumed. However, complete removal of oxygen, either by continued irradiation or by deæration beforehand, markedly influenced the course of the reaction.

The most probable initial reaction is addition of an OH radical, produced by irradiation, to the ethylene double bond:

$$OH + CH_2{:}CH_2 \longrightarrow HO{\cdot}CH_2{\cdot}CH_2{\cdot} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

This type of reaction has been well established from polymerisation studies;[10] the alternative reaction, suggested by Henley *et al.*,[2] *viz.*,

$$OH + CH_2{:}CH_2 \longrightarrow H_2O + CH_2{:}CH{\cdot} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2a)$$

[4] Kolthoff and Lingane, " Polarography," Vol. 2, p. 552 (New York, 1952).
[5] Weiss, *Nature*, 1944, **153**, 748.
[6] Allen, Hochanadel, Ghormley, and Davis, *J. Phys. Chem.*, 1952, **56**, 575.
[7] Johnson and Weiss, *Proc. Roy. Soc.* 1957, *A.*, **240**, 189.
[8] Hochanadel and Lind, *Ann. Rev. Phys. Chem.*, 1957, **7**, 83.
[9] Johnson, Scholes, and Weiss, *Nature*, 1956, **177**, 883.
[10] Dainton, *J. Phys. Colloid Chem.*, 1948, **52**, 490.

XUM

is unlikely on energetic grounds (cf. Walsh [11]). In the absence of oxygen, addition of hydrogen atoms to ethylene may also occur:

$$H + CH_2{:}CH_2 \longrightarrow CH_2{\cdot}CH_3 \quad \ldots\ldots\ldots\ldots (3)$$

The radicals formed in reactions (2) and (3) may react with monomeric ethylene resulting in polymerisation, and the oily polymer observed in absence of oxygen is presumably so formed. Oxidation of the radical formed in reaction (2), which may occur to some extent as an alternative to reaction of the radical with ethylene, could yield, for example, acetaldehyde:

$$HO{\cdot}CH_2{\cdot}CH_2{\cdot} \xrightarrow{\text{(oxidation)}} [HO{\cdot}CH_2{\cdot}CH_2{\cdot}]^+ \longrightarrow CH_3{\cdot}CHO + H^+ \quad \ldots\ldots (4)$$

Oxidative termination of the polymerisation could produce higher aldehydes (butyraldehyde, etc.). The enhancement of the aldehyde yields at low pH suggests that the species H_2^+ may be involved in the oxidation step.[12] The effect of ferric ion, which increases the yield of acetaldehyde, is attributable to the enhancement of reaction (4) at the expense of the polymerisation (cf. Dainton [13]). No detailed study of these reactions has been made.

Oxygen in the irradiated solution qualitatively alters the course of the reaction: it will add to hydrogen atoms and to the free radical formed in reaction (2):

$$H + O_2 \longrightarrow HO_2 \quad \ldots\ldots\ldots\ldots (5)$$

$$HO{\cdot}CH_2{\cdot}CH_2{\cdot} + O_2 \longrightarrow HO{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}O{\cdot} \quad \ldots\ldots\ldots\ldots (6)$$

If one molecule of oxygen is required for the formation of each molecule of organic product and of hydrogen peroxide, the extent of oxygen consumption would correspond to $G(O_2) = 7{\cdot}4$ at pH 1·2, and $G = 4{\cdot}2$ at pH 5·5 [these figures allow for a " molecular yield " of hydrogen peroxide of $G^{\text{w}}(H_2O_2) = 0{\cdot}8$, which would be formed without using any oxygen]. The observed values for oxygen utilisation at pH 5·5, *viz.*, $G(O_2) = 4{\cdot}0$, is in quite good agreement with the above assumption and this confirms also that the measured products are the only ones formed here. At pH 1·2 the agreement between the observed value, *viz.*, $G(O_2) = 6{\cdot}0$, and that calculated is less satisfactory. There are no reasons to believe that the products at this pH are different; rather does this discrepancy reflect some ambiguity regarding the molecular oxygen consumption in the formation of acetaldehyde, whose yield is greater at the lower pH. While reaction (7) followed by some reduction step would require one molecule of O_2 per acetaldehyde molecule, formation of acetaldehyde *via* the radical $\cdot CH_2{\cdot}CH_2{\cdot}OH$ (eqn. 2), with subsequent dehydrogenation by O_2 to give HO_2, would proceed without net consumption of molecular oxygen. The experimental values for consumption of oxygen lie in each case within the calculated limits derived from these two routes; *i.e.*, for pH 1·2, $G(O_2)$ ~5·0—7·5 and for pH 5·5 $G(O_2)$ ~3·9—4·2. The relatively high total yield of organic product ($G \simeq 5{\cdot}9$, at pH 1·2) is greater than the maximum value which may be assumed for $G(OH)$ ($\gtrsim 3{\cdot}6$) under these conditions. The occurrence of a short-chain reaction, involving primary attack by OH radicals only, could lead to a total yield greater than that corresponding to $G^{\text{w}}(OH)$, but is unlikely in view of the observed small dependence of the yield on ethylene concentration. Therefore, it appears that the high yields, particularly in acid solution, are associated with attack on ethylene by either hydrogen atoms and/or HO_2 radicals:[14]

$$CH_2{:}CH_2 + H \longrightarrow CH_2{\cdot}CH_2{\cdot} \xrightarrow{O_2} CH_2{\cdot}CH_2{\cdot}O_2{\cdot} \quad \ldots\ldots\ldots (7)$$

$$CH_2{:}CH_2 + HO_2 \longrightarrow HO_2{\cdot}CH_2{\cdot}CH_2{\cdot} \xrightarrow{O_2} HO_2{\cdot}CH_2{\cdot}CH_2{\cdot}O_2{\cdot} \quad \ldots\ldots (8)$$

Even in the presence of oxygen, certain organic solutes can, under suitable conditions, compete for the hydrogen atoms produced in the radiolysis.

[11] Walsh, *Trans. Faraday Soc.*, 1946, **42**, 282.
[12] Weiss, *Nature*, 1950, **165**, 728.
[13] Collinson, Dainton, and McNaughton, *Trans. Faraday Soc.*, 1957, **53**, 489.
[14] Hargrave and Morris, *ibid.*, 1956, **52**, 89.

XUM

The observed products, glycollaldehyde, acetaldehyde, and formaldehyde, presumably arise from mutual oxidation–reduction reactions between the possible primary species $HO{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}O$ and $HO{\cdot}O{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}O$, but little is known about the reactions of such radicals. These reactions appear to be markedly influenced by the pH of the irradiated solutions. Yields of the primary products from water are probably pH-dependent. Also, participation of hydrogen atoms and/or the HO_2 radical may lead to pH-dependent reactions owing to the different possibilities for reaction of this radical and its anion O_2^- ($HO_2 \rightleftharpoons H^+ + O_2^-$) and to the equilibrium $H + H^+ \rightleftharpoons H_2^+$.

The formation of formaldehyde from ethylene is of interest, since this process is somewhat analogous to the radiation-induced formation of mucondialdehyde from benzene [15] and of formylkynurenin from tryptophan.[16] The opening of a double bond, *i.e.*, $(>C{=}C<) \longrightarrow (>C{=}O) + (O{=}C<)$, appears to be a general reaction under these conditions, and apparently occurs only in the presence of molecular oxygen.

From ethylene solutions irradiated in the presence of ferrous salt, the major product is formaldehyde, with smaller quantities of acetaldehyde. The most probable mode of formation of formaldehyde under these conditions involves reactions (2) and (6) followed by:

$$HO{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}O{\cdot} + Fe^{2+} (+ H^+) \longrightarrow HO{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}OH + Fe^{3+} \quad (9)$$

$$HO{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}OH + Fe^{2+} \longrightarrow HO{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot} + OH^- + Fe^{3+} \quad (10)$$

$$HO{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot} \longrightarrow HO{\cdot}CH_2{\cdot} + H{\cdot}CHO \quad (11)$$

$$HO{\cdot}CH_2{\cdot} + O_2 \longrightarrow HO{\cdot}CH_2{\cdot}O{\cdot}O{\cdot} \quad (12)$$

$$HO{\cdot}CH_2{\cdot}O{\cdot}O{\cdot} + Fe^{2+} (+ H^+) \longrightarrow HO{\cdot}CH_2{\cdot}O{\cdot}OH + Fe^{3+} \quad (13)$$

$$HO{\cdot}CH_2{\cdot}O{\cdot}OH + Fe^{2+} \longrightarrow HO{\cdot}CH_2{\cdot}O{\cdot} + OH^- + Fe^{3+} \quad (14)$$

$$HO{\cdot}CH_2{\cdot}O{\cdot} + Fe^{2+} (+ H^+) \longrightarrow H{\cdot}CHO + H_2O + Fe^{3+} \quad (15)$$

Reactions (9) and (10) are analogous to those assumed to explain the effect of certain other organic solutes in increasing the yield of ferrous oxidation.[17,18] Reaction (11), which involves fission of the C–C bond, is similar to a reaction assumed by Hawkins [19] to explain the formation of dodecane-2 : 11-dione from 2-ethyl*cyclo*pentyl hydroperoxide by reduction with ferrous sulphate solution.

Formation of acetaldehyde under these conditions can be most readily accounted for by reaction (8) followed by:

$$HO{\cdot}O{\cdot}CH_2{\cdot}CH_2{\cdot} + Fe^{2+} \longrightarrow Fe^{3+} + OH^- + CH_3{\cdot}CHO \quad (16)$$

In order to obtain more information on this point, the products were studied under conditions where OH radicals but not HO_2 radicals are formed. A solution of ethylene–oxygen (3 : 1 in the gas phase; total pressure 1 atm.; pH = 1·2) containing ferrous sulphate (10^{-3}M) was treated with a solution containing 7×10^{-6} moles of hydrogen peroxide. Analysis of the aldehydes formed, by chromatography of their dinitrophenylhydrazones, showed the presence of formaldehyde but not acetaldehyde. This suggests that the HO_2 radical may be essential for the formation of acetaldehyde in this system.

According to the suggested mechanism, the presence of ethylene should result in an increase in the ferrous oxidation yield equivalent to $2\{G(H{\cdot}CHO) - G(CH_3{\cdot}CHO)\}$ above the yield in its absence [*i.e.*, $G(Fe^{3+}) = 15{\cdot}5$]. For the measured values of $G(H{\cdot}CHO) = 3{\cdot}8$ and $G(CH_3{\cdot}CHO) = 1{\cdot}2$, this would give $G(Fe^{3+}) = (15{\cdot}5 + 5{\cdot}2) = 20{\cdot}7$, a value somewhat lower than the measured $G(Fe^{3+}) \sim 23$. This can be easily deduced as follows: In the absence of ethylene one OH produces one Fe^{3+}; in the presence of ethylene (and oxygen), according to reaction (9)—(15), one OH gives five Fe^{3+}, with the simultaneous

[15] Daniels, Scholes, and Weiss, *J.*, 1956, 832.
[16] Jayson, Scholes, and Weiss, *Biochem. J.*, 1954, **57**, 386.
[17] Dewhurst, *Trans. Faraday Soc.*, 1952, **48**, 905.
[18] Johnson, Scholes, and Weiss, *J.*, 1953, 3091.
[19] Hawkins, *J.*, 1955, 3463.

XUM

formation of 2 H·CHO; thus there is a net increase of 4 Fe^{3+} per OH with the simultaneous formation of 2 H·CHO, *i.e.*, additionally formed 2 Fe^{3+} per 1 H·CHO.

One HO_2 yields 3 Fe^{3+} in the absence of ethylene; in the presence of ethylene, one HO_2 gives [*via* the intermediate $HO{\cdot}O{\cdot}CH_2{\cdot}CH_2$ formed according to equation (8) followed by reaction (16)] one Fe^{3+} leading to the formation of one $CH_3{\cdot}CHO$. Thus we have a net decrease of 2 Fe^{3+} per $CH_3{\cdot}CHO$ formed.

Experimental

Preparation of Solutions.—Ordinary distilled water was distilled from alkaline potassium permanganate and then from dilute phosphoric acid. The pH of the pure water was 5·5 and was adjusted to lower pH values by adding sulphuric acid.

Etnylene and oxygen (British Oxygen Co. Ltd.; medical grade) were used directly from the cylinders.

(i) *Irradiations at* 1 *Atm. Pressure.*—The solutions were prepared and irradiated in cylindrical " Pyrex " glass vessels fitted with a side-arm and a tap. The vessel, containing 50 ml. of water, and the apparatus used for preparing the gas solutions were deærated by repeated pumping with a 2-stage oil pump and shaking. For experiments in its presence, oxygen gas was then admitted to the required pressure (mercury manometer) and the irradiation vessel filled thereat. The apparatus was then pumped out, and ethylene admitted to a pressure of 1 atm. and the vessel was filled to the required pressure with ethylene. For experiments in the absence of oxygen, before the vessel was filled, the ethylene was condensed in a liquid nitrogen trap and freed from any non-condensable gases by repeated pumping and melting. After the vessels had been filled, the solutions were allowed to become saturated with the gas by standing for at least 12 hr., with occasional shaking.

(ii) *Irradiations at Higher Pressures.*—The irradiations were carried out in a steel " bomb " fitted with a screw cap and two valves (Fig. 1). A " Pyrex " glass vessel containing water was placed inside the " bomb " and the ethylene and oxygen were admitted to the required pressure. Saturation was brought about by shaking for at least 12 hr.

Determination of Ethylene.—A solution of potassium bromide and potassium bromate was added to an aliquot part of the ethylene solution and to an equal volume of water. After acidification with sulphuric acid, the excess of bromine in each solution was determined by adding an excess of a potassium bromide solution and measuring the absorption of the Br_3^- ion at 265 mμ. The ethylene concentration was calculated from the difference between the absorptions of the two solutions by use of a calibration curve prepared by measuring the absorption of standard bromine solutions.

Irradiation Arrangements.—We used a 500 Curie ^{60}Co γ-ray source of the type described by Ghormley and Hochanadel.[20] The dose rate, measured by the ferrous sulphate dosimeter (assuming 15·5 molecules of ferric ion to be formed per 100 ev of energy absorbed), was $1{\cdot}0 \times 10^{-7}$ (ev/N) ml.$^{-1}$ min.$^{-1}$.

Identification and Determination of the Products.—(i) Hydrogen peroxide was identified and determined by the titanium sulphate reagent.[21]

(ii) Organic hydroperoxides do not, in general, react with titanium sulphate reagent but oxidise iodide and react with ferrous thiocyanate. Determination of total peroxide in the irradiated solutions by means of potassium iodide [22] and by ferrous thiocyanate [23] showed, under certain conditions, the presence of an organic hydroperoxide in addition to hydrogen peroxide. The identity of the hydroperoxide has not been established, the yields always being too low. Its rate of reaction with iodide was measured and found to be practically identical with that of hydrogen peroxide, whereas methyl hydroperoxide and ethyl hydroperoxide (prepared by the methods of Rieche [24] and Minkoff,[25] respectively) reacted much more slowly under the same conditions.

[20] Ghormley and Hochanadel, *Rev. Sci. Instr.*, 1951, **22**, 473.
[21] Eisenberg, *Ind. Eng. Chem. Anal.*, 1943, **15**, 327.
[22] Hochanadel, *J. Phys. Chem.*, 1952, **56**, 587.
[23] Egerton, Everett, Minkoff, Rudrakanchana, and Salooja, *Analyt. Chim. Acta*, 1954, **10**, 422.
[24] Rieche and Hitz, *Ber.*, 1929, **62**, 2458.
[25] Minkoff, *Proc. Roy. Soc.*, 1954, *A*, **224**, 176.

XUM

(iii) Formaldehyde and acetaldehyde were identified as their 2 : 4-dinitrophenylhydrazones, their ethanolic solutions being used for paper chromatography according to Meigh.[26]

For determination of total aldehyde, Johnson and Scholes's [27] method was used. The ratio (formaldehyde/acetaldehyde) was determined by running, on a paper chromatogram, a solution of the dinitrophenylhydrazones of the irradiation products, eluting the developed spots into 5 ml. of ethanol, and comparing the absorption of the solutions at 360 mμ in a Unicam spectrophotometer. The concentrations of acetaldehyde and formaldehyde in the irradiated solutions were calculated from the expressions:

$$[\text{acetaldehyde}] = D/\{RE(\text{H·CHO}) + E(\text{CH}_3\text{·CHO})\}$$

and [formaldehyde] = R[acetaldehyde], where D = total optical density determined by Johnson and Scholes's method, R = [H·CHO]/[Me·CHO], and E(H·CHO) and E(Me·CHO) are the molar extinction coefficients of the formaldehyde and acetaldehyde dinitrophenylhydrazones, respectively, as determined by Johnson and Scholes's method.

(iv) Glycollaldehyde with dinitrophenylhydrazine gives glyoxal dinitrophenylhydrazone which, like other dialdehyde hydrazones, gives a purple-blue colour in strongly alkaline solution. Since this dinitrophenylhydrazone is relatively insoluble in carbon tetrachloride, benzene was used to extract it from the aqueous solution. The irradiated solution was treated with dinitrophenylhydrazine reagent and extracted with benzene; addition of ethanolic sodium hydroxide to the extract gave a blue colour, indicating the presence of either glyoxal or glycollaldehyde in the irradiated solution. The absorption spectrum of the alkaline ethanol–benzene solution was identical with that of glyoxal dinitrophenylhydrazone under the same conditions.

That one of the irradiation products was glycollaldehyde (not glyoxal) was shown by the method of Dechary *et al.*[28] This depends upon the formation of a coloured derivative when solutions of this carbonyl compound are treated with 2 : 3-diaminophenazine reagent. Glyoxal reacts in acetic acid solution, but glycollaldehyde only under conditions where conversion into glyoxal can occur, *i.e.*, in concentrated sulphuric acid.

We thank the United Kingdom Atomic Energy Authority Research Group, Harwell, for support and for permission to publish this paper; also the Research Works Department of Imperial Chemical Industries Limited, Billingham Division, for valuable help in the design and construction of the vessel for the pressure experiments.

KING'S COLLEGE, NEWCASTLE UPON TYNE, 1. [*Received, November 4th*, 1957.]

[26] Meigh, *Nature*, 1952, **170**, 577.
[27] Johnson and Scholes, *Analyst*, 1954, **77**, 937.
[28] Dechary, Kun, and Pitot, *Analyt. Chem.*, 1952, **26**, 449.

---

444. N-*Oxides and Related Compounds. Part XII.* Infrared Spectra of Some Carbonyl Compounds.*

By A. R. KATRITZKY, A. M. MONRO, and (in part) J. A. T. BEARD, D. P. DEARNALEY, and N. J. EARL.

The positions of the carbonyl stretching band in esters and ketones show that the pyridine 1-oxide ring can release electrons to the 4-position more easily than to the 3-position, but that the reverse is true of the pyridine ring.

All the bands in a monosubstituted pyridine or oxide may be correlated with those of other compounds containing either (*a*) the same nucleus or (*b*) the same substituent. Positions and apparent extinction coefficients of bands characteristic of carbonyl compounds are treated statistically, and tentative assignments are made.

PREVIOUS papers in this series recorded dipole moments which indicated that the ring in pyridine 1-oxide,[2] but not the ring in pyridine–boron trichloride,[3] could release electrons

* Part XI, Hands and Katritzky, *J.*, 1958, 1754.

[1] For general review see Katritzky, *Quart. Rev.*, 1956, **10**, 395.
[2] Part IV, Katritzky, Randall, and Sutton, *J.*, 1957, 1769.
[3] Parts VIII and IX, Bax, Katritzky, and Sutton, *J.*, 1958, 1254, 1258.

XUM

to a substituent in the 4-position. To gain more evidence on this point, and to investigate 2- and 3-substituted compounds, in which non-linearity makes interpretation of dipole moments difficult, we have studied the infrared spectra of methyl and ethyl esters and methyl ketones. Carbonyl compounds were selected because they have already been

TABLE 1. *Ethyl esters.*

		1		2		3		4		5		6		7	
		CO		Chain		Et, CH_3 scissor		Et, CH_2 bend (as)		Et, CH_2 bend (s)		Et, CH_2 wag		CCO	
No.	Ring †	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A
Compounds X·CO_2Et															
1	Ph	1716	360	—		1467 *	30	(—)		1391	30	1369	90	1313	120
2	4P ª	1730	360	—		1465	25	1445	25	1393 *	45	1370	105	1326	135
3	3P	1724	360	—		1470	30	1447	25	1392	30	1370	100	1328	60
4	2P	1723	280	—		1465 ‡	55	(—)		1390	35	1369	115	1305	450
5	4PO	1722	390	—		1470 *	60	(—)		1390	35	1369	125	1303	270
6	3PO	1732	340	—		1468 *	55	(—)		1394	30	1370	110	1298 ‡	560
7	2PO	1741	260	—		1464	40	(—)		1391	25	1369	75	—	
8	4PBCl$_3$	1739	290	—		1460	35	(—)		1390	35	1370	110	1325	90
9	4PBBr$_3$	1739	330	—		1469	30	1447 *	35	1397	30	1371	100	1326	100
10	3PBCl$_3$	1737	360	—		1464	50	(—)		1393	35	1371	110	1321	100
Compounds X·CH_2·CO_2Et															
11	Ph	1730	330	1415 *	25	1465 *	25	(—)		1391	20	1369	75	1325	55
12	4P	1736	270	(—)		1465 *	15	1450 *	20	1390	20	1370	75	1325 *	55
13	3P	1730	310	(—)		(—)		1444	35	1391	30	1367	85	1327	70
14	3PO	1737	360	1420 *	35	(—)		(—)		1395	30	1370	90	1334	70
Compounds X·CH_2·CH_2·CO_2Et															
15	Ph	1730	330	1415	30	(—)		(—)		1391 *	35	1373	90	1340	40
16	4P	1731	330	(—)		1465 *	25	1445 *	45	(—)		1374	90	1339	45
17	3P	1731	320	(—)		(—)		1447	45	1391 *	35	1375	85	1345	40
Compounds X·CH:CH·CO_2Et															
18	Ph	1711	380	1640	220	1465 *	25	(—)		1390	30	1369	110	1328	150
19	4P	1715	350	1648	85	1465	25	1445	25	1392	30	1367	105	1335	70
20	3P	1715	350	1646	150	(—)		1447	25	1390	25	1368	90	1335	30
21	2P	1712	370	1648	85	(—)		(—)		1392	25	1368	95	1317	290
22	4PO	1715	350	1644	140	(—)		(—)		1389	30	1368	100	1319 *	260
23	3PO	1715	330	1650	85	(—)		(—)		1391	30	1368	100	1319	270
24	2PO	1715	320	1639	65	1468 *	35	(—)		1392	35	1369	95	—	
25	4PBCl$_3$ ª	1723	425	1638	270	($CHCl_3$)		($CHCl_3$)		1390 *	40	1369	130	1336	70
Compounds X·CO_2Et															
1	1277	530	1249 *	100	1174	70	1110	230	1100 *	130	1028 ‡	140	—	870	<15
2	1282	530	1249 *	90	1174	25	1120	170	1095	35	1018	65	—	871	25
														851	30
3	1284	500	(—)		1167	35	1128 *	160	1086 *	40	1027 ‡	170	—	853	15
							1110	205							
4	1293	250	1244	200	1171	50	1135 *	185	1087	65	1015	45	—	852	25
							1125	240							
5	1284 *	280	1258 ‡	570	(—)		1120	125	1091 *	85	1015	95	—	(—)	
6	(—)		(1232	200)	(—)		1108	220	1077	30	1014 ‡	230	—	861	20
7	1311	270	(—)		1175 *	55	1132	175	1094 ‡	120	1011	45	—	878 *	35
							1112 *	45						866	40
8	1283	500	1245	95	1170	20	1130	90	1091 *	60	1010	75	—	870	60
							1115 *	50						855	35
9	1285	490	1240	90	1175	30	1139 *	90	1093 *	45	1012	70	—	870	55
							1132	95						856	35
							1119 *	55							
10	1302	360	1258	55	1173	60	1133	190	(—)		1010	75	—	857	65
							1117	190							
Compounds X·CH_2·CO_2Et															
11	1296	90	1250	120	1155	130	1140 *	130	1094	30	1028 ‡	130	—	—	
12	1300	75	1256	110	1156	95	1136 *	80	1095	25	1028	100	—	—	
13	1300	75	1256	125	1153	120	1138 *	110	1094	40	1027 ‡	180	—	—	
14	1303 *	105	(—)		1156 ‡	350	(—)		1093	25	1027	145	—	—	

TABLE 1. (*Continued.*)

	8		9		10		11		12		13		14		15	
	CCO				CO·O				Et		OEt		HC:CH		?	
No.	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A
Compounds X·CH_2·CH_2·CO_2Et																
15	1297	90	1257	90	1180	125	1159 1149 *	125 110	1094	40	1035 1015	85 50	—		—	
16	1296	90	1247 *	105	1182	135	1151	105	1094	30	1034 1018	60 40	—		855	20
17	1299	85	1252 *	100	1183	150	1154	90	1097 *	40	1034 * 1019 *	70 40	—		—	
Compounds X·CH:CH·CO_2Et																
18	1310	280	1271	180	1179	310	—		1094	45	1033	105	980	115	882 860	20 40
19	1310 1297 *	300 190	1266	145	1175	230	—		1093	30	1028	95	981 957 *	150 20	842	20
20	1311	290	1268	155	1175	200	—		1094	30	1025 ‡	110	981	110	880 865	20 25
21	1299	260	1266	140	1161	170	—		1092 ‡	55	1029	100	981	120	872	<15
22	1311	270	(—)		1177 *	330	—		1093	55	1032 ‡	185	978	155	884	15
23	1303	160	(—)		1179	260	—		1093	30	1030	115	977	160	875 * 836	15 15
24	1309	300	1242	200	1184	200	—		1094	30	1031 *	95	982	90	902	20
25	1309	390	($CHCl_3$)		($CHCl_3$)		—		(—)		1027	110	978 968	165 60	($CHCl_3$)	

* Shoulder.

† Abbreviations used are: P = pyridine. PO = pyridine 1-oxide. $PBCl_3$ = pyridine–boron trichloride. $PBBr_3$ = pyridine–boron tribromide. Preceding numerals denote position of substituent.

‡ Peak considered to be formed by the superimposition of two bands, which will consequently appear twice. — Absence of band. (—) Band is masked by other stronger absorption. ($CHCl_3$) Band masked by solvent.

[a] Other band at 3310 cm.$^{-1}$ (20) (overtone?). [b] 0·02M-Solution in 1 mm. cell.

extensively studied (for reviews see refs. 4*a*, 5*a*) and it is well established that in a given series the C=O stretching frequency decreases as the electron-releasing power of an attached group increases.[4a, 5a] For consistency the spectra were all measured at 0·2M-concentration in chloroform in a 0·117 mm. cell. The bands could be divided into those characteristic of the nucleus and those characteristic of the substituent. This paper records the latter; the nuclear bands will be discussed elsewhere,[6] together with those of rings containing other substituents, with which excellent correlations are shown. Bands ($\varepsilon \geqslant 15$) characteristic of neither nucleus nor substituent, of which there are few, are indicated by lettered footnotes.

Chloroform was used because more compounds are soluble in it than in, *e.g.*, carbon disulphide or carbon tetrachloride. In a 0·1 mm. cell only the bands at 3020—3000, 1240—1200 and below 805 cm.$^{-1}$ are obscured by solvent absorption.[4c] Apparent molecular extinction coefficients are recorded; they are comparable between themselves, although considerably different from the true molecular extinction coefficients, both because of the variation of ε_A with concentration,[7, 8] and because of the finite slit widths used;[4d, 7] in addition, corrections have not been made for absorption by the finite mole fraction of solvent displaced,[4e] and the difference in densities [4e] and refractive indices [4f] of solvent and solution; there are also other sources of error.[4g] Also at 0·2M-concentration

[4] Jones and Sandorfy in Weissberger, "Technique of Organic Chemistry, Vol. IX. Chemical Applications of Spectroscopy," Interscience Publ. Inc., London, 1956: (*a*) p. 443 ff., (*b*) p. 473 ff., (*c*) p. 300, (*d*) p. 273, (*e*) p. 265, (*f*) p. 263, (*g*) p. 269, (*h*) p. 471, (*i*) pp. 369, 374, 377 ff., (*j*) p. 502 ff., (*k*) p. 482.

[5] Bellamy, "The Infrared Spectra of Complex Molecules," Methuen, London, 1956: (*a*) p. 114—163, (*b*) p. 119 ff., (*c*) p. 21, (*d*) p. 161 ff., (*e*) p. 163.

[6] Katritzky *et al.*, following papers; Katritzky, Coates, Beard, Hands, and Lagowski, to be published.

[7] Thompson, *Spectrochim. Acta*, 1956, **9**, 133.

[8] Jones, *ibid.*, p. 235.

in the 0·117 mm. cell, values outside the range 50—250 will be very approximate, because they correspond to optical densities outside the optimum range for measurement. The

TABLE 2. *Methyl esters.*

		1 CO		2 Chain		3 OMe CH_3 bend (s)		4 CCO		5 CCO		6 CCO	
No.	Ring	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A
Compounds X·CO_2Me													
26	Ph	1724	370	—		1437	100	1315	140	1279	480	1250 *	65
27	4P	1735	390	—		1440	120	1327	160	1286	540	1254 *	75
28	3P	1730	370	—		1438	90	1328	65	1285	370	(—)	
29	2P	1730	340	—		1446	135	1310	310	1294	190	1246	190
30	4PO	1727	390	—		1437	140	1304	270	(—)		1261 ‡	600
31	3PO	1741	360	—		1442 ‡	270	1307 ‡	570	(—)		(1236	230)
32	2PO	1749	260	—		1442	240	—		1317	260	(—)	
33	4PBCl$_3$	1745	340	—		1439 *	180	1325	110	1291	500	1242	80
34	3PBCl$_3$	1745	420	—		1441 ‡	250	1324 *	130	1304	450	1255	35
Compounds X·CH_2·CO_2Me													
35	Ph	1735	310	1418 *	25	1439	95	1341	60	1299	65	1255	110
36	4P	1740	300	(—)		1440	90	1346	50	1300	60	1260	110
Compounds X·CH_2·CH_2·CO_2Me													
37	Ph	1731	320	1418 *	25	1440	110	1365	60	1295	75	1260 *	80
38	4P •	1732	280	(—)		1438	110	1365	50	1310 * / 1295	55 / 80	1260 *	80
Compounds CH:CH·CO_2Me													
39	Ph	1714	350	1640	200	1436	90	1330	195	1315	210	1278	200
40	4P	1718	360	1648	85	1435	115	1337	120	1312 / 1297	320 / 170	1278	180

		7 CO·O		8 CO·O		9 ?		10 OMe		11 CH:CH		12 ?	
No.	Ring	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A
Compounds X·CO_2Me													
26	Ph	1192 * / 1175	50 / 65	1114	195	1100 *	75	967	30	—		823	<15
27	4P	1192 *	60	1124	210	—		967	60	—		850	30
28	3P	1188 ‡	50	1112 *	140	1085	25	960	20	—		825	30
29	2P	1193 *	85	1128	220	1089 ‡	45	966	40	—		833	25
30	4PO	(—)		1122	100	1091	50	964	65	—		—	
31	3PO	1192 *	70	1109	220	1080 *	25	983	85	—		(—)	
32	2PO	(—)		1136	220	1094 ‡	90	958	25	—		815	<15
33	4PBCl$_3$	(—)		1130 / 1121 *	105 / 45	—		960	70	—		870	30
34	3PBCl$_3$	1192 ‡	70	1135	250	1081 *	60	960	25	—		—	
Compounds X·CH_2·CO_2Me													
35	Ph	1158	125	1140 *	105	—		1013	60	—		—	
36	4P	1156	95	1140 *	85	—		1012	50	—		—	
Compounds X·CH_2·CH_2·CO_2Me													
37	Ph	1194	90	1160	110	—		1028 ‡ / 987	35 / 30	—		—	
38	4P •	1191	90	1170	110	—		1023 / 981	20 / 35	—		832 / 810	25 / 45
Compounds CH:CH·CO_2Me													
39	Ph	1187 * / 1172	125 / 290	—		—		1039 / 1014	40 / 45	987 * / 980	65 / 110	863	45
40	4P	1190 * / 1170	110 / 270	—		—		1035 / 1010	50 / 30	980 / 955	150 / 15	859 / 842	20 / 20

* Other band at 1339 cm.$^{-1}$ (35). See also footnotes to Table 1.

standardised conditions under which the spectra were measured are given on p. 2191. ε_A was reproducible with a standard deviation of about 8%.

The Carbonyl Stretching Band.—(i) When a carbonyl group is directly attached to the ring, a definite pattern of changes is observed. All the heterocyclic compounds have

higher C=O stretching frequencies than the corresponding benzene derivative; the increments in wave numbers are shown in Table 5. As the differences were small, the position of the CO band for the ethyl esters was also measured at 5 times the normal resolution; the results were within ± 2 cm.$^{-1}$ of those obtained in the normal way.

TABLE 3. *Methyl ketones.*

		1 CO		2 Me?		3 Me		4		5 ·CCO		6		7 ?		8 Me?	
No.	Ring	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A
41	Ph[a]	1680	290	1420	30	1358	135	1309 1295	25 25	1264	290	1245 *	70	(—)		954	45
42	4P[b]	1700	230	(—)		1361	135	1322	20	1263	310	1242 *	105	1082	15	960	25
43	3P	1690	340	(—)		1359	130	—		1270	280	($CHCl_3$)		1089	25	956	45
44	2P	1695	240	1417	25	1358	165	1297	70	1283	160	(1234	105)	1087 *	<15	954	45
45	4PO	1692	260	(—)		1359	150	1300	85	1280 *	130	(—)		1080	15	959	55
46	3PO	1707	190	(—)		1361	115	1295 *	240	(—)		($CHCl_3$)		1084	30	961	15
47	2PO	1691	220	(—)		1357	115	—		1300	190	(1235	140)	1075	30	968	15

[a] Other band at 1177 cm.$^{-1}$ (20). [b] Shoulder at 1146 cm.$^{-1}$ (50). See also footnotes to Table 1.

TABLE 4. *Aldehydes.*

		1 CH str.		2		3 CO str.		4 ?		5 δCH		6 ?		7 ?		8 γCH	
No.	Ring	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A
48	Ph[a]	2850	35	2740	35	1705	350	1652	30	1389	20	1309	75	1165	70	828	120
49	4P	2840	25	2750	<15	1721	280	1674	30	1388	35	1322	85	1190	65	835	50
50	3P	2850	30	2740	20	1712	370	1667 *	30	1388	40	1326	55	1190 *	35	832	100
51	2P	2830	30	2740 *	<15	1717	300	1656 *	20	1365	25	1294	20	($CHCl_3$)		832	100

[a] Other band at 1195 cm.$^{-1}$ (20). See also footnotes to Table 1.

TABLE 5. *Carbonyl stretching bands. Increments in wave numbers over that for the corresponding benzenoid compound.*

	4P	3P	2P	4PO	3PO	2PO	4PBCl$_3$	3PBCl$_3$
CO_2Et	14	8	7	6	16	25	23	21
CO_2Et[a]	14	8	10	9	18	28	24	25
CO_2Me	11	6	6	3	17	25	21	21
COMe	20	10	15	12	27	11	—	—
CHO	16	7	12	—	—	—	—	—

[a] Differences obtained at high resolution. The CO frequency in ethyl benzoate was 1714. See also footnote † to Table 1.

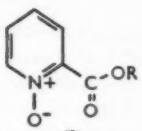
For 3- and 4-substituted compounds, in each series, the increments are in the order: Ph < 4-pyridyl 1-oxide ~ 3-pyridyl < 4-pyridyl < 3-pyridyl 1-oxide < 3- or 4-position of pyridine–boron trichloride. Thus the rings should have electron-releasing ability in the stated positions in the opposite order. This agrees with evidence from dipole moments,[2,3] ultraviolet spectra,[9] and chemical reactivity (electrophilic reagents attack pyridines in the 3-, but pyridine 1-oxides in the 4-position [1]), and with theoretical predictions. In no important canonical form of pyridine 1-oxide does a negative charge appear at the 3-position, and inductive effects make the 1-oxide less able than the pyridine to release electrons at that position. The ring of pyridine–boron trichloride is still less able to release electrons in both the 3- and the 4-position.

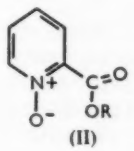
Consideration of the 2-substituted compounds is more difficult owing to possible steric hindrance (in the 1-oxides) and direct field effects. The increments for the 2-substituted pyridine 1-oxide esters are much greater than for 2-acetylpyridine 1-oxide. This may be because both the planar configurations (I and II) of the ester are unfavoured owing to steric and direct field effects, but the ketone can adopt the configuration (III) with

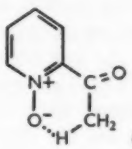
[9] Katritzky and Monro, unpublished work.

XUM

possibly a weak hydrogen bond. The reluctance of pyridine oxides to undergo electrophilic substitution in the 2-position is probably due to the direct field effect.[1] Electron-availability at the 2-position in pyridines appears to be intermediate between that in the 3- and the 4-position.


(I)


(II)


(III)

(ii) For compounds $X{\cdot}CH_2{\cdot}CO_2Et$, the effect seems to persist weakly, for the frequencies are in the order: Ph ~ 3-pyridyl < 4-pyridyl ~ 3-pyridyl 1-oxide; but in compounds $X{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2Et$ the position of the CO band is constant at 1731 cm.$^{-1}$ and in compounds $X{\cdot}CH{:}CH{\cdot}CO_2Et$ it is relatively constant at 1715 cm.$^{-1}$, somewhat lower, as expected,[4b] than the 1735 and 1720 cm.$^{-1}$ recorded in non-polar solvents for fatty and αβ-unsaturated esters respectively.[4a]

(iii) The intensities of the carbonyl bands are in the ranges: ethyl esters (260—390) [(335 ± 35)]; * methyl esters (260—420) [(340 ± 45)]; methyl ketones (190—340) [(250 ± 50)]; and aldehydes (280—370). These values are lower than those which were recorded for similar compounds when a calcium fluoride prism was used [10] (*e.g.*, $Ph{\cdot}CH_2{\cdot}CO_2Et$ 540, $Ph{\cdot}CO_2R$ *ca.* 700 [10c]), but they agree with Cross and Rolfe's measurements [11] with sodium chloride optics ($Ph{\cdot}COMe$ 310, $R{\cdot}CO_2R$ *ca.* 350, Ph·CHO 320).

The 3000 *cm.*$^{-1}$ *Region.*—Of the CH stretching bands, because of solvent interference,[6] the sodium chloride prism resolved only the band due to the hydrogen atom of the CHO group; in each of the aldehydes a doublet was found near 2850 and 2750 cm.$^{-1}$ (⩽40) (Table 4, cols. 1 and 2); such doublets have been observed and discussed for other aldehydes by Pinchas.[12]

The 1650 *cm.*$^{-1}$ *Region.*—(i) Compounds $X{\cdot}CH{:}CH{\cdot}CO_2Et$ (Table 1, col. 2) and $X{\cdot}CH{:}CH{\cdot}CO_2Me$ (Table 2, col. 2) show the C:C stretching band at 1651—1638 [1644 ± 4] cm.$^{-1}$; it had been reported [4i] that for the C:C band in αβ-unsaturated ketones the intensity increased and the position was lowered by *ca.* 30 cm.$^{-1}$, from the 1678—1668 cm.$^{-1}$ of unconjugated compounds. The intensity and frequency (cm.$^{-1}$) of the bands are in the order:

				4-Pyridyl				3-Pyridyl				2-Pyridyl
Ph		3-Pyridyl		1-oxide		4-Pyridyl		1-oxide		2-Pyridyl		1-oxide
220	>	150	~	140	>	85	~	85	~	85	>	65
1640	<	1646	~	1644	<	1649	~	1650	~	1648	>	1639

thus it appears that the greater the electron-donating power of the ring, the greater is the intensity of the band, and the lower its frequency (*i.e.*, the greater the single-bond character). The frequency for the 2-substituted pyridine oxide, and the frequency and intensity for the 4-substituted pyridine–boron trichloride are out of line with this generalisation; possibly here receipt of electrons by the ring from the double bond becomes of overriding importance.

The bands for the two available compounds $X{\cdot}CH{:}CH{\cdot}CO_2Me$ agree well with those for corresponding ethyl esters.

* Values in parentheses are apparent molecular extinction coefficients. Values in square brackets are arithmetical means and standard deviations, calculated by omitting those compounds where the band is present as a shoulder, and, in the case of ε_A, those in which it is superimposed on another band or measured in a 1 mm. cell.

[10] (*a*) Jones, Ramsay, Keir, and Dobriner, *J. Amer. Chem. Soc.*, 1952, **74**, 80; (*b*) Marion, Ramsay, and Jones, *ibid.*, 1951, **73**, 305; (*c*) Hampton and Newell, *Analyt. Chem.*, 1949, **21**, 914.

[11] Cross and Rolfe, *Trans. Faraday Soc.*, 1951, **47**, 354.

[12] Pinchas, *Analyt. Chem.*, 1957, **29**, 334.

XUM

(ii) The aldehydes show a weak band or shoulder (Table 4, col. 4) at 1674—1652 cm.$^{-1}$ (20—30), possibly due to contamination by the corresponding acid.

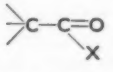
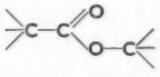
The 1500—1350 *cm.*$^{-1}$ *Region.*—Previous workers have noticed that intensities of methyl and methylene C–H deformations are enhanced when the groups are near an oxygen atom,[5c,13] and we confirm this.*

(i) Where these frequencies are at >1410 cm.$^{-1}$ they are overlapped by nuclear bands,[6] and interpretation of the spectrum can be difficult; but the known [13,14] asymmetrical bending vibrations of CO_2Me groups at 1446—1435 cm.$^{-1}$ (90—140 except for the 2-pyridyl 1-oxide derivative where it is overlapped) [1439 ± 3 cm.$^{-1}$ (116 ± 15)] is easily distinguished (Table 2, col. 3). In methyl acetate the band occurs at 1435 cm.$^{-1}$ (130).[15] The ethyl esters show weaker bands at 1470—1460 cm.$^{-1}$ (25—50) and 1447—1444 cm.$^{-1}$ (25—45) (Table 1, cols. 3 and 4), corresponding respectively to the scissors methylene vibration and the asymmetrical bending of the (ethoxy) methyl group found by Jones and Nolin [16] at respectively 1464 (35) and 1446 cm.$^{-1}$ (40) for ethyl acetate. For the only two methyl ketones where the region is not obscured, bands are found at 1420—1417 cm.$^{-1}$ (25—30) (Table 3, col. 2). Weak bands or shoulders at 1418—1415 cm.$^{-1}$ are sometimes found for the esters $X{\cdot}CH_2{\cdot}CO_2R$ and $X{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2R$ (Table 1, col. 2; Table 2, col. 2).

(ii) The known methyl CH deformation for acetyl groups (ref. 13, at *ca.* 1364 cm.$^{-1}$; ref. 17, at 1370 cm.$^{-1}$) was found at 1361—1357 cm.$^{-1}$ (115—165) [1359 ± 1·5 cm.$^{-1}$ (135 ± 20)] (Table 3, col. 3).

(iii) The ethyl esters show bands at 1397—1389 cm.$^{-1}$ (20—35) [1391·5 ± 2 cm.$^{-1}$ (30 ± 5)] and 1375—1367 cm.$^{-1}$ (75—125) [1370 ± 2 cm.$^{-1}$ (100 ± 10)] (Table 1, cols. 5 and 6), corresponding respectively to the (ethoxy) methyl symmetrical bending and methylene wagging modes found by Nolin and Jones [16] at respectively 1393 (35) and 1359 cm.$^{-1}$ (60) for ethyl acetate; the latter was found at *ca.* 1372 cm.$^{-1}$ by Francis [13] for some simple ethyl esters.

(iv) The aldehydes show a weak band at 1389—1365 cm.$^{-1}$ (20—40) (Table 4, col. 5), which is probably the CH in-plane deformation mode shown in Raman spectra as a strong band at *ca.* 1390 cm.$^{-1}$.[18]

(IV)   (V)

The 1350—1240 *cm.*$^{-1}$ *Region.*—The absorption in this region is assigned to the group (IV) because corresponding methyl and ethyl esters show almost identical absorption there (Table 1, cols. 7—9; Table 2, cols. 4—6) and the absorption of the methyl ketone (IV; X = C instead of O) is similar (Table 3, cols. 4—6), but that of the aldehydes is very different (Table 4, col. 6). The absorption depends on the environment of the carbon atom to which the carbonyl group is attached. Interpretation of this region in the oxides is sometimes difficult because of overlap with the intense $N^+–O^-$ band. Strong absorption by esters has been found previously in this region,[4f,5d] and assigned to C–O stretching modes. Where the acid radical is kept constant and the alkyl radical changed the position of the band varies inversely with that of the C=O stretching band;[4g] this is neither expected nor found in our compounds.

(i) Compounds $X{\cdot}CH_2{\cdot}CO_2Et$ and $X{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2Et$ and the corresponding methyl esters all show three bands, which steadily increase in intensity towards lower frequencies.

* In γ-picoline oxide the intensity of the CH_3 symmetrical deformation is <10, but in α-picoline oxide it is 25, doubtless owing to the proximity of the $N^+–O^-$ group (Katritzky, Beard, and Monro, unpublished observations).

[13] Francis, *J. Chem. Phys.*, 1951, **19**, 942.
[14] Jones, Cole, and Nolin, *J. Amer. Chem. Soc.*, 1952, **74**, 5648, 5662.
[15] Nolin and Jones, *Canad. J. Chem.*, 1956, **34**, 1382.
[16] *Idem*, *ibid.*, p. 1392.
[17] Thompson and Torkington, *J.*, 1945, 640.
[18] Kohlrausch, " Ramanspecktren," Becker and Erler, Leipzig, 1943, pp. 281—282.

The first band is at 1365 cm.$^{-1}$ for X·CH_2·CH_2·CO_2Me, at 1346—1341 cm.$^{-1}$ for X·CH_2·CO_2Me, at 1345—1339 cm.$^{-1}$ for X·CH_2·CH_2·CO_2Et, and at 1334—1325 cm.$^{-1}$ for X·CH_2·CO_2Et; the intensities are all (40—70) [(55 ± 10)]. All the compounds show the other bands at 1300—1295 cm.$^{-1}$ (60—90) [1298 ± 2 cm.$^{-1}$ (80 ± 10)] and at 1260—1250 cm.$^{-1}$ (90—125) [1256 ± 3 cm.$^{-1}$ (110 ± 10)]. The first of these three bands may be due to a wagging mode of the group adjacent to the carbonyl, which shows at 1356 cm.$^{-1}$ in methyl propionate and at 1347 cm.$^{-1}$ in ethyl propionate.[13]

(ii) Compounds X·CO_2Et, X·CO_2Me, X·CH:CH·CO_2Et, and X·COMe also show in general three bands in this region; the positions and intensities depend in a regular way both on the ring and on the substituent. Absorption in the two compounds X·CH:CH·CO_2Me available closely resembles that in the corresponding compounds X·CH:CH·CO_2Et.

(*a*) The first of these bands for compounds X·CO_2Me, X·CH:CH·CO_2Et, and X·COMe are respectively at the following positions relative to that for X·CO_2Et: 0—5 [1·5 ± 1·5] higher, 7—15 [10·5 ± 3] higher and 3—8 [5 ± 2] cm.$^{-1}$ lower, and 0·69—1·22 [1·06 ± 0·19], 0·50—1·25 [0·80 ± 0·30], and 0·15—0·31 [0·21 ± 0·07] times as intense. If the benzenoid compounds (intensity 120—150 in the esters, 25 in the ketone) are taken as standards, the bands in the corresponding 3- and 4-pyridyl derivatives and their boron trichloride compounds are 7—15 [11 ± 3] cm.$^{-1}$ higher and of intensity (30—160) [(90 ± 40)] for the esters and (20) for the ketone. For the 2-pyridyl and 4- and 3-pyridyl 1-oxide derivatives the bands are 5—15 [10 ± 3] cm.$^{-1}$ lower and of intensity (270—450) [310 ± 80] for the esters and *ca.* (80) for the ketones.

(*b*) The second band is at a relatively constant position 1311—1299 [1308 ± 4] cm.$^{-1}$ and intensity (160—300) [265 ± 50] in the compounds X·CH:CH·CO_2Et. The in-plane *trans*-CH=CH deformation mode would be expected in this region, but the band is weak, at least in non-conjugated olefins.[19]

Fluctuations in position and intensity are again parallel for compounds X·CO_2Et, X·CO_2Me, and X·COMe. Bands for corresponding compounds in the last two series are respectively at positions 1—8 [3½ ± 2½] cm.$^{-1}$ higher, and 10—19 [13 ± 3] cm.$^{-1}$ lower than, and of intensity 0·74—1·25 [0·95 ± 0·17] and 0·55—0·70 [0·61 ± 0·06] times, those of the X·CO_2Et series.

In compounds X·CO_2Et, X·CO_2Me, and X·COMe the position relative to the corresponding phenyl compound varies in the order: 2-pyridyl 1-oxide 34—38, 3-pyridyl–boron trichloride 24—25, 2-pyridyl 15—19, 4-pyridyl–boron trichloride 6—12, 3-pyridyl 6—7, and 4-pyridyl −1 to 7 wavenumbers higher. The intensities for methyl and ethyl pyridine-2-carboxylate and their oxides are (190—280) [(240 ± 35)], and for the ketones (160—190); whereas in the 3- and 4-pyridyl series, as well as for their boron chloride compounds and the phenyl series, the esters have an intensity of (360—540) [(475 ± 65)], and the ketones (280—310).

(*c*) The third band is too often obscured by solvent or N^+–O^- absorption for any definite conclusions to be legitimate about its position or intensity.

(iii) The aldehydes show a single band at 1326—1294 cm.$^{-1}$ (20—85).

The 1200—1100 *cm.*$^{-1}$ *Region.*—Absorption in this region is assigned to the group (V), for ketones do not absorb here, and aldehydes show merely a single band at *ca.* 1190 cm.$^{-1}$ (≤70) (Table 4, col. 7), but the absorption in corresponding methyl and ethyl esters is very similar (Table 1, cols. 10 and 11; Table 2, cols. 7 and 8).

(i) Compounds X·CH:CH·CO_2R (R = Et and Me) show one band at 1184—1161 cm.$^{-1}$ (170—310) [1174 ± 7 cm.$^{-1}$ (240 ± 50)]. A band at 1200—1100 cm.$^{-1}$ has been reported for unsaturated esters.[5e]

(ii) Compounds X·CH_2·CO_2R (R = Et and Me) show a band at 1158—1153 cm.$^{-1}$ (95—130) [1155 ± 2 cm.$^{-1}$ (110 ± 15)] which has a shoulder at 1140*—1136* cm.$^{-1}$ (80—130).

(iii) Compounds X·CH_2·CH_2·CO_2Et show two bands at 1183—1180 cm.$^{-1}$ (125—150)

[19] Sheppard and Simpson, *Quart. Rev.*, 1952, **6**, 1.

and 1159—1151 cm.$^{-1}$ (90—125); these two bands are shown by the compounds X·CH_2·CH_2·CO_2Me at *ca.* 10 cm.$^{-1}$ higher frequencies, but have very similar intensities.

(iv) Compounds X·CO_2Et show a band at 1175—1170 cm.$^{-1}$ (20—70) [1172 ± 3 cm.$^{-1}$ (40 ± 20)] which is at higher frequencies (⩾1188) in compounds X·CO_2Me and is partly obscured by solvent absorption. Compounds X·CO_2Me and X·CO_2Et absorb at 1136—1108 cm.$^{-1}$ (100—275) [1123 ± 10 cm.$^{-1}$ (180 ± 55)]; the peak for the former is at 0—4 cm.$^{-1}$ above that for the latter and has 0·80—1·30 [1·07 ± 0·17] times the intensity. The peaks for these ethyl esters often show a shoulder.

The 1100—1080 *cm.*$^{-1}$ *Region.*—In this region (Tables 1—3, cols. 12, 9, and 7 respectively), all the ethyl esters and ketones show a peak at respectively 1095—1077 cm.$^{-1}$ (25—65) [1092 ± 4 cm.$^{-1}$ (35 ± 10)] and 1089—1075 cm.$^{-1}$ (15—30) [1082 ± 5 cm.$^{-1}$ (25 ± 10)], which is present only for those methyl esters with the group directly attached to the ring, and not all of these. The band is possibly present in spectra of the other methyl esters at intensities too low to be distinguished. Ethyl acetate shows a band at 1097 cm.$^{-1}$ (40).[16]

The 1040—950 *cm.*$^{-1}$ *Region.*—(i) The *trans*-CH:CH CH deformation of compounds X·CH:CH·CO_2R (R = Me and Et) occurs at 982—977 cm.$^{-1}$ (90—165) [980 ± 2 cm.$^{-1}$ (130 ± 25)] (Table 1, col. 14; Table 2, col. 11); in simple *trans*-olefins it occurs at 980—965 cm.$^{-1}$ (50—150).[4i]

(ii) The ketones show a band at 968—954 cm.$^{-1}$ (15—55) [959 ± 5 cm.$^{-1}$ (35 ± 15)] (Table 3, col. 8).

(iii) All the ethyl esters have a band at 1035—1010 cm.$^{-1}$ (45—145) (Table 1, col. 13), but the position and intensity is more exactly defined for each type; thus compounds X·CH_2·CO_2Et and X·CH:CH·CO_2Et have the band at 1028—1027 cm.$^{-1}$ (100—145) and 1033—1027 cm.$^{-1}$ (95—115) [1029 ± 3 cm.$^{-1}$ (105 ± 10)] respectively; and for compounds X·CH_2·CH_2·CO_2Et a main band is found at 1035—1034 cm.$^{-1}$ (60—85) and a subsidiary one at 1018—1015 cm.$^{-1}$ (40—50). The relative positions of the band for compounds X·CO_2Et are Ph (1028 cm.$^{-1}$) > 3- > 4- > 2-pyridyl ~ 4- > 3- > 2-pyridyl 1-oxide ~ 3- ~ 4-pyridyl–boron trichloride (1010 cm.$^{-1}$), which is the order of electron-withdrawing ability of the ring;[2,3] the intensity is (45—95) [(70 ± 15)].

(iv) The corresponding band for the methyl esters is presumably that in Table 2, col. 10. For compounds X·CO_2Me it appears at 983—958 cm.$^{-1}$ (20—85) [965 ± 8 cm.$^{-1}$ (45 ± 25)]; there is no simple dependence of position on the electron-withdrawing ability of the ring. The band occurs at considerably higher frequencies in spectra of the other compounds, and as a doublet for X·CH_2·CH_2·CO_2Me (cf. X·CH_2·CH_2·CO_2Et). A band at 980 cm.$^{-1}$ (20) has been reported [15] for methyl acetate.

The 900—800 *cm.*$^{-1}$ *Region.*—(i) The aldehydes show the CH out-of-plane deformation band at 835—828 cm.$^{-1}$ (50—120) (Table 4, col. 8), in the range 975—825 cm.$^{-1}$ given by Colthup.[20]

(ii) One or two weak bands of unknown origin are found for many ethyl (Table 1, col. 15) and some methyl esters (Table 2, col. 12) at 880—850 cm.$^{-1}$ (⩽65).

Conclusions.—The 1400—800 cm.$^{-1}$ region of the spectrum has been shown to be much more amenable to quantitative treatment than was previously suspected. Apparent extinction coefficients are reproducible and comparable when measured under standard conditions, and are shown to be of great value to the interpretation of the spectrum in terms of structural groups.

Experimental

Preparation of Compounds.—The pyridine-aldehydes and most of the benzenoid compounds were redistilled commercial products; the others were prepared by standard methods. The

[20] Colthup, *J. Opt. Soc. Amer.*, 1950, **40**, 379.

preparations of most of the pyridines and 1-oxides have already been reported;[3, 6, 21] compounds were recrystallised or redistilled before measurement.

2-Ethoxycarbonylpyridine 1-Oxide.—Hydrogen chloride was passed 6 hr. through picolinic acid 1-oxide (4·5 g.) in boiling ethanol [100 c.c.; dried over $Mg(OEt)_2$]. Volatile material was removed at 100°/15 mm., the residue added to water (50 c.c.) at 0°, and the whole basified with aqueous sodium carbonate and extracted with chloroform (5 × 30 c.c.). Distillation of the dried extracts gave the *ester oxide* (0·15 g., 3%), b. p. 170—180° (bath)/0·4 mm. (Found: C, 57·6; H, 5·7. $C_8H_9O_3N$ requires C, 57·5; H, 5·4%).

The *methyl ester oxide* was similarly prepared (3%, but 60% of acid recovered), b. p. 175—180° (bath)/0·1 mm. (Found: C, 54·8; H, 4·7. $C_7H_7O_3N$ requires C, 54·9; H, 4·6%). The compound has been reported [22, 23] as an intermediate, but not characterised.

Attempts to prepare the above compounds by oxidation of the pyridine esters by peracetic acid failed.

Boron Halide Complexes.—The following were made by the method given in Part VIII:[3] *4-ethoxycarbonylpyridine–boron tribromide*, prisms, m. p. 97—98°, from ethanol (Found: N, 3·5; Br, 59·7. $C_8H_9O_2NBr_3B$ requires N, 3·5; Br, 59·7%); *3-ethoxycarbonyl-*, m. p. 64—65°, from ethanol (Found: C, 36·0; H, 3·8. $C_8H_9O_2NCl_3B$ requires C, 35·8; H, 3·4%); *4-(2-ethoxycarbonylvinyl)-*, rhombs, m. p. 202—204°, from ethanol (Found: C, 40·4; H, 4·2. $C_{10}H_{11}O_2NCl_3B$ requires C, 40·8; H, 3·8%); *4-methoxycarbonyl-* (87%), prisms, m. p. 115—117°, from ethanol (Found: C, 32·9; H, 2·8; N, 5·3. $C_7H_7O_2NCl_3B$ requires C, 33·1; H, 2·8; N, 5·5%); *3-methoxycarbonyl-pyridine–boron trichloride* (54%), prisms, m. p. 113—114°, from ethanol (Found: C, 33·1; H, 2·8; N, 5·5%).

Preparation of Oxides.—Oxidation of the corresponding pyridine with peracetic acid gave: 4-methoxycarbonyl-, m. p. 116·5—118·5°, from ethyl acetate (lit.,[24] 118—119°); 3-methoxycarbonyl-, m. p. 97—98°, from ethyl acetate (lit.,[25] m. p. 97°; [23] m. p. 101—102°), and *2-acetylpyridine 1-oxide*, b. p. 82° (bath)/0·3 mm. (Found: C, 61·6; H, 5·3. $C_7H_7O_2N$ requires C, 61·3; H, 5·2%) [*picrolonate*, prisms (from ethanol), changing to needles at 109°, then melting at 157° (Found: C, 50·4; H, 3·9. $C_{17}H_{15}O_7N_5$ requires C, 50·9; H, 3·8%)].

Measurement of Spectra.—A Perkin-Elmer model 21 instrument was used with the following settings: gearing 2″ per micron; mechanical speed belt at bottom but one position; electrical speed 4; no auto-suppression (*i.e.*, speed 20 min. per run); gain 7·7; mechanical response 1; electrical response 1; light source 0·34 amp.; slit programme 4 (*i.e.*, resolution at 1600, 1400, 1250, 1100, and 850 $cm.^{-1}$ was respectively 8·0, 5·5, 4·7, 3·8, 2·6 wave numbers). A sodium chloride prism was used.

The work described in this and the four following papers was done during the tenure (by A. R. K.) of an I.C.I. Fellowship, and we are greatly indebted to Mrs. A. J. D. Katritzky for much help with the computation, to Dr. M. C. Whiting and other colleagues in Oxford for their interest in this work, to Mr. G. Taylor for comments on the statistical treatment, and to Dr. N. Sheppard for very helpful discussion. The spectra were measured by Mr. F. Hastings and Mrs. W. Sheldon (under Dr. Strauss's supervision).

THE DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, December 5th*, 1957.]
[*Present address* (A. R. K.).—UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE.]

[21] (*a*) Part II, Katritzky, *J.*, 1956, 2404; (*b*) Parts VII and X, Katritzky and Monro, *J.*, 1958, 150, 1263; (*c*) Katritzky, *J.*, 1955, 2581, 2586.
[22] Newbold and Spring, *J.*, 1949, S 133.
[23] Shimizu, Naito, Ohta, Yoshikawa, and Dohmori, *J. Pharm. Soc. Japan*, 1952, **72**, 1474; *Chem. Abs.*, 1953, **47**, 8077.
[24] Yale, Losee, Martins, Holsing, Perry, and Berstein, *J. Amer. Chem. Soc.*, 1953, **75**, 1933.
[25] Clemo and Koenig, *J.*, 1949, S231.

XUM

445. N-*Oxides and Related Compounds. Part XIII.*[1] *Infrared Spectra of 4-Substituted Pyridine 1-Oxides.*

By A. R. Katritzky and J. N. Gardner.

In addition to bands due to the substituent, twenty-four 4-substituted pyridine 1-oxides showed, with few exceptions, ten characteristic bands in chloroform; their variations in intensity and position with the nature of the substituent are discussed.

In previous Parts of this series the NH stretching region of infrared spectra was used in studies of potentially tautomeric amines,[2] and the carbonyl stretching region was used in studies of the conjugating power of various nuclei.[1] Arising out of this work, measurement under standard conditions of monosubstituted benzenes, pyridines, pyridine 1-oxides, and pyridine–boron trichloride complexes has shown that (with few exceptions): (i) in any one compound the bands (with $\varepsilon_A \geqslant 15$) are characteristic of either (*a*) all compounds with the same nucleus or (*b*) all compounds with the same substituent; and (ii) the number, position, and intensity of the bands characteristic of any one nucleus or substituent are either reasonably constant, or vary in a regular manner with the electronic (and/or steric?) character of the nucleus to which the substituent is attached, or of the substituent to which the nucleus is attached.

This paper and the succeeding one discuss the bands characteristic of 4- and 2-substituted pyridine 1-oxides. Apparent molecular extinction coefficients are recorded (cf. ref. 1, where reference is made to the errors and approximations involved).

The infrared spectra of 4-monosubstituted pyridine 1-oxides have been little investigated previously. Costa and Blasina [3] discussed the variation of the position of the $^+N{-}O^-$ band in the chloro-, methoxy-, and nitro-compounds in Nujol mulls and carbon disulphide solution; the amino- and hydroxy-compounds were insoluble in suitable solvents and this hindered interpretation.[4] The methyl and ethyl compounds were measured by Shindo [5] in part of a general investigation of alkylpyridine 1-oxides; 4-picoline 1-oxide has also been measured.[6] In so far as our results are comparable with this work, good agreement is found, considering the change of state or solvent.

The 3000 *cm.*$^{-1}$ *Region.*—The sodium chloride prism resolves one band only at 3010—2940 cm.$^{-1}$ (50—145) [2980 ± 16 cm.$^{-1}$ (110 ± 23)].* As pointed out by Wiley and Slaymaker,[6] *N*-oxides in chloroform solution absorb hereabouts because hydrogen bonding lowers the solvent CH stretching frequency so that it is no longer compensated; absorption in this region is less for the corresponding pyridine which should form weaker hydrogen bands, and very weak or absent in the non-bonded pyridine–boron trihalide complexes.[7] In agreement, the band becomes on the average less intense, and occurs at slightly higher frequencies, on going from electron-donor to electron-acceptor substituents.

The 1600 *cm.*$^{-1}$ *Region.*—The position of the single band (col. 2) varies from 1647 to 1609 cm.$^{-1}$ as the substituent changes from strongly electron-donating to strongly electron-attracting: an exception is the bromo-compound (No. 18) absorbing at 1605 cm.$^{-1}$; a heavy atom attached directly often lowers the frequency of a nuclear band.[7] The pyridine 1-oxide nucleus can either accept or release electrons at the 4-position,[2,8] and this is probably why the intensity of this band depends on the magnitude of the conjugative

* For the significance of parentheses and brackets see Part XII (footnote p. 2187).[1]

[1] Part XII, Katritzky, Monro, Beard, Dearnaley, and Earl, preceding paper.
[2] Part V, Gardner and Katritzky, *J.*, 1957, 4375.
[3] Costa and Blasina, *Z. phys. Chem.* (*Frankfurt*), 1955, **4**, 24.
[4] Costa, Blasina, and Sartori, *ibid.*, 1956, **7**, 123.
[5] Shindo, *Pharm. Bull.* (*Japan*), 1956, **4**, 460.
[6] Wiley and Slaymaker, *J. Amer. Chem. Soc.*, 1957, **79**, 2233.
[7] Katritzky and co-workers, unpublished results.
[8] Part IX, Katritzky, Randall, and Sutton, *J.*, 1957, 1769.

XUM

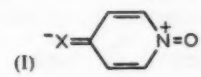
ability of the substituent and not on its type. For 4-substituted pyridines, where the nucleus conjugates effectively only with electron-donating substituents,[2,8] the corresponding band is intensified by such substituents, but weakened by electron-accepting substituents.[7]

The 1500—1400 *cm.*$^{-1}$ *Region.*—Two bands are found. That of higher frequency (col. 3) is at 1492—1470 [1483 ± 6] cm.$^{-1}$, except for the amines (Nos. 1 and 2) where it is considerably higher, and for the halogen compounds (Nos. 17 and 18) where it is lower (cf. above). For the compounds without a strongly electron-withdrawing substituent (Nos. 1—19) the intensity is (170—420) [(260 ± 70)]; for the others it is lower (100—120) except for the nitro-compound (250).

The other band (col. 4) occurs at 1456—1431 [1443 ± 7] cm.$^{-1}$; interpretation of the variable intensity (20—140) is difficult because of overlap with aliphatic CH deformations of the substituents. Absorption for, *e.g.*, the halogen compounds, and comparison with that of other nuclei shows that a nuclear bands does indeed occur here.

The 1300—1240 *cm.*$^{-1}$ *Region.*—The strong $^{+}N-O^{-}$ stretching frequency already reported[3,5] is obscured by solvent absorption for compounds with strongly electron-donating substituents (Nos. 1—5). The frequency is raised by electron-accepting substitutents; as pointed out elsewhere,[3,5] this is because canonical forms as (I) become important and increase the double-bond character of the $^{+}N-O^{-}$ linkage. The intensities are (220—400) [(310 ± 55)], and tend to increase with increasing electron-withdrawing ability of the substituent.

The 1200—1000 *cm.*$^{-1}$ *Region.*—One band (col. 6) is at 1181—1159 [1169 ± 5] cm.$^{-1}$; for amines and ethers (Nos. 1—5) the intensity is relatively low (65—80), for the esters (Nos. 19, 21, 22) it is high (420—510), otherwise it is (110—320) [(200 ± 50)].



(I)

(II)

A second band (missing from the spectrum of the dimethylamino-compound) is at 1118—1089 [1101 ± 7] cm.$^{-1}$; except for the halogeno-compounds (Nos. 17, 18) (which often have more intense nuclear bands in this region [7]) and the ethoxy- and methoxy-carbonyl compounds (strong overlap with substituent bands) the intensity is (5—35) [(20 ± 10)].

A third band is at 1044—1023 cm.$^{-1}$ (30—85) [1033 ± 5 cm.$^{-1}$ (55 ± 15)]; the frequency seems to be lowered somewhat by both strongly electron-donating and electron-attracting substituents.

The 800 *cm.*$^{-1}$ *Region.*—Two bands are generally found; probably one is a ring hydrogen deformation, and the other corresponds to the band at 838 cm.$^{-1}$ (220) for pyridine oxide itself: a band in this region was originally assigned to the $^{+}N-O^{-}$ stretching frequency; [9] it has been found in the spectrum of pyrimidine oxides.[6] The bands occur at 860—842 cm.$^{-1}$ (15—270) [852 ± 6 cm.$^{-1}$ (75 ± 60)] and at 855—820 cm.$^{-1}$ (50—250) [836 ± 9 cm.$^{-1}$ (180 ± 55)] and are considered to be superimposed in spectra of Nos. 15, 21, and 22.

Assignments.—Randle and Whiffen's work on *para*-substituted benzene derivatives [10] suggests the assignments given at the head of the Table. The mean positions of the bands are within about 20 wave-numbers in the two groups of compounds; the main difference is that there are no bands in the spectra of 4-substituted pyridine 1-oxides corresponding to those at [1571 ± 11] and [961 ± 12] cm.$^{-1}$ for the *para*-substituted benzene derivatives. It is not yet possible to compare intensities in the two groups of compounds.

This work supports the conclusion [1] that 4-methylaminopyridine 1-oxide exists as such and not in the imino-form (II).

[9] Ito and Hata, *Bull. Chem. Soc. Japan*, 1955, **28**, 353.
[10] Randle and Whiffen, Paper No. 12, Report on Conference on Molecular Spectroscopy 1954, Institute of Petroleum.

XUM

		1 [a] $CHCl_3$ νCH		2 A_g νCC / νCN		3 B_{2u} νCC / νCN		4 B_{2u} νCC / νCN		5 — ν^+N–O$^-$	
No.	Subst.	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A
1	NHMe	2960	120	1647	135	1525 1498 *	170 120	1431	50	1194	80
2	NMe_2	2940	135	1642	140	1517	280	1447 ‡	165	(1230	80)
3	OMe	2970	145	1635	60	1492	250	1440 ‡	135	(1232	165)
4	OEt	2960	120	1636	60	1491	250	1448 ‡	50	(1215	175)
5	O·CH_2Ph	2970	130	1629	45	1485 ‡	360	1456 ‡	105	(1220	160)
6	NMe·COMe	2980	105	1625	65	1483	420	1440	65	1248	260
7	NMe·COPh	3000	135	1626 *	110	1487 ‡	520	1451 ‡	100	1248	310
8	Me	2980	140	1622	5	1486	200	1442	20	1247	220
9	Et	2980	115	—		1484	190	1450	60	1242	230
10	CH_2·CH_2Ph	2960	115	(—)		1487 ‡	280	1451 ‡	90	1243	250
11	CH_2Ph	2960	100	(—)		1485 ‡	280	1450 ‡	80	1243	260
12	CH_2·C_6H_4·NO_2-*p*	2970	90	(—)		1484 ‡	310	1449	75	1246	260
13	C:CPh [b]	3000	125	(—)		1475	195	1445 ‡	50	1260	370
14	CH:CHPh	2980	100	1620 *	15	1485	300	1452 ‡	75	1251	340
15	Ph	2980	85	1622 *	15	1473	210	1431	35	1248	270
16	S·CH_2Ph	2990	130	(—)		1488	285	1435	95	1246	300
17	Cl	2990	115	—		1464	215	1438	85	1251	300
18	Br	2970	95	1605	30	1461	350	1432	100	1250	320
19	CH:CH·CO_2Et	2990	120	1618	115	1487	280	1449	140	1258	400
20	CN [c]	($CHCl_3$)		1615	150	1472	110	($CHCl_3$)		1282	350
21	CO_2Et	2980	125	1616	155	1483	120	1445	110	1258 ‡	570
22	CO_2Me	2980	75	1616	115	1484	100	1444	110	1261 ‡	600
23	COMe [d]	2990	95	1611	190	1481	100	1438	55	1253	390
24	NO_2 [e]	3010	50	1609	210	1470	250	1442 *	30	1294 1283	400 400

		6 A_g βCH		7 B_{2u} βCH		8 B_{2u} βCH		9 — ? $^+$N–O$^-$		10 B_{1u} γCH	
No.	Subst.	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A
1	NHMe	1176	80	1095	5	1029	55	853	35	825	145
2	NMe_2	1181 ‡	120	—		1030	70	845 *	40	829 818	170 180
3	OMe	1168	75	1099	15	1027 ‡	290	856	50	835	230
4	OEt	1169	70	1102 *	20	1029 *	145	855	75	838	185
5	O·CH_2Ph	1166	65	1099	15	1026 *	115	857	15	834	240
6	NMe·COMe	1165	115	(—)		1030	55	844	145	836 *	110
7	NMe·COPh	1172	175	(—)		1044	45	860	15	843	200
8	Me	1173	170	1112	5	1041	60	855	75	828	200
9	Et	1170	175	1110	10	1038	55	850	80	839	185
10	CH_2·CH_2Ph	1171	220	1098	10	1038	50	844	65	832 824 *	100 70
11	CH_2Ph	1170	220	1098	15	1039	50	858	55	844 813	50 40
12	CH_2·C_6H_4·NO_2-*p*	1171	230	1100	25	1037	40	860	90	828	80
13	C:CPh [b]	1170	220	1095	25	1032 ‡	130	842	270	820	155
14	CH:CHPh	1168	260	1095	15	1032 ‡	110	860	70	844 824	15 130
15	Ph	1172	185	1100	15	1036	40	844 ‡	190	844 ‡	190
16	S·CH_2Ph	1175	220	1110	25	1034	70	844	100	827	155
17	Cl	1168	180	1116	55	1033	30	845	60	834	225
18	Br	1167	200	1118 1089	40 60	1032	35	849 *	20	840 832	65 240
19	CH:CH·CO_2Et	1165	500	1105	35	1032 ‡	185	855	25	836 815	250 65
20	CN [c]	1163	240	1097	20	1029	50	($CHCl_3$)		($CHCl_3$)	
21	CO_2Et	1159	510	1104	90	1030 *	50	855 ‡	165	855 ‡ 835	165 25
22	CO_2Me	1160	420	1102	50	1030	45	855 ‡	195	855 ‡	195
23	COMe [d]	1164	320	1100	15	1029	80	849 *	100	843	210
24	NO_2 [e]	1168	110	1089	30	1023	85	(—)		852	220

* Shoulder. ‡ Absorption considered to be the superimposition of two peaks. — Absence of absorption. (—) Band masked by stronger absorption. ($CHCl_3$) Band masked by solvent.

[a] Tentative assignments of symmetry and type of vibration (cf. ref. 10) are given directly under the column numbers. [b] Extra band shown at 1145 cm.$^{-1}$ (85). [c] Measured at 0·01M-concentration in a 1 mm. cell because of low solubility. [d] Extra band shown at 1542 cm.$^{-1}$ (15). [e] Band at 1609 cm.$^{-1}$ is split, with another component at 1589 cm.$^{-1}$ (135).

Experimental

Preparation of Materials.—The preparation of most of the compounds has already been described.[1, 2, 8, 11] Compounds were recrystallised or distilled immediately before measurement.

4-*Benzylthiopyridine* 1-*Oxide.*—4-Chloropyridine 1-oxide was added gradually to ethanolic sodium benzyl sulphide (from 1·24 g. of toluene-ω-thiol with sodium ethoxide from 0·23 g. of sodium and 15 c.c. of ethanol). The mixture was refluxed for 45 min. Solid carbon dioxide was added, the whole filtered, and the filtrate evaporated. The residue was taken up in chloroform, centrifuged, and again evaporated, to give the *oxide* (1·0 g., 46%), yellowish plates (from ethyl acetate), m. p. 147—149° (Found: C, 66·0; H, 5·2; N, 6·4; S, 14·5. $C_{12}H_{11}ONS$ requires C, 66·3; H, 5·5; N, 6·4; S, 14·8%).

4-Ethylpyridine, oxidised by peracetic acid in the normal way, gave the 1-oxide (84%), deliquescent prisms (from ethyl acetate), m. p. 106—109° (Found: C, 68·3; H, 7·5. Calc. for C_7H_9ON: C, 68·3; H, 7·4%) (lit.,[12] m. p. 100—120°).

Measurement of Spectra.—A Perkin-Elmer Model 21 instrument was used, with a sodium chloride prism, slit programme 4, and the settings previously [1] given. The compounds were measured in purified chloroform in a 0·117 mm. cell, at 0·2M-concentration.

The Dyson Perrins Laboratory, Oxford University. [*Received, January 14th,* 1958.]

[11] See also Katritzky and his co-workers, *J.*, 1956, 2063, 2404; 1957, 191, 4385; 1958, 150, 1263.
[12] Shimizu, Naito, Ohta, Yoshikawa, and Dohmori, *J. Pharm. Soc.* (*Japan*), 1952, **72**, 1474; *Chem. Abs.*, 1953, **47**, 8077.

---

446. N-*Oxides and Related Compounds. Part XIV.*[1] *Infrared Spectra of 2-Substituted Pyridine* 1-*Oxides.*

By A. R. Katritzky and A. R. Hands.

The positions and intensities of twelve characteristic bands are recorded and discussed for twenty-four 2-substituted pyridine 1-oxides.

After our work [1] on 4-substituted pyridine 1-oxides we report the spectra of some 2-analogues. Only the 2-methyl compound had been investigated previously.[2,3]

The 3000 *cm.*$^{-1}$ *Region.*—The hydrogen-bonded chloroform CH stretching frequency [1] is found at 3010—2950 cm.$^{-1}$ (40—175) [2985 ± 15 cm.$^{-1}$ (95 ± 30)].

The 1650—1550 *cm.*$^{-1}$ *Region.*—The main band (col. 2 of the Table) is at 1640—1596 cm.$^{-1}$. Electron-donors tend to raise, and electron-attracting groups and heavy atoms (S, Cl) to lower, the frequency. Intensity variation is also significant; electron-donors increase markedly the low values observed with saturated substituents (*e.g.*, No. 11). Increase of the intensity by electron-acceptors is less (contrast 4-substituted pyridine 1-oxides [1]; cf. the reluctance of pyridine 1-oxides to release electrons at the 2-position [4, 5]).

A second band sometimes found (col. 3) is strong only with electron-donating substituents; in the amido-compounds it is stronger than the band just discussed. The position is 1577—1550 cm.$^{-1}$ except for the esters.

The 1500—1400 *cm.*$^{-1}$ *Region.*—Two bands are shown. The first (col. 4) occurs above 1500 cm.$^{-1}$ for the ether and amines (Nos. 1—5), otherwise at 1500—1470 cm.$^{-1}$ [1483 ± 9]. Its intensity falls from *ca.* (200) in the compounds with strongly electron-donating substituents (except No. 1 where the band is split) to low values for electron-attractors; chlorine and sulphur here appear to act as electron-donors.

[1] Part XIII, Katritzky and Gardner, *J.*, 1958, 2192.
[2] Shindo, *Pharm. Bull.* (*Japan*), 1956, **4**, 460.
[3] Wiley and Slaymaker, *J. Amer. Chem. Soc.*, 1957, **79**, 2233.
[4] Katritzky, Monro, Beard, Dearnaley, and Earl, *J.*, 2182.
[5] Hands and Katritzky, *J.*, 1754.

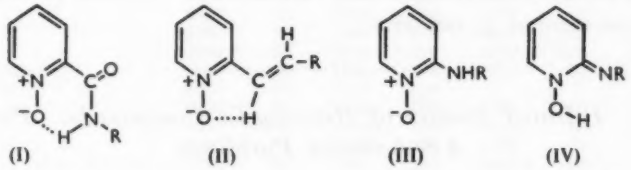
XUM

No.	Subst.	1 [a] $CHCl_3$ νCH cm.$^{-1}$	ε_A	2 A_1 νCC/νCN cm.$^{-1}$	ε_A	3 B_1 νCC/νCN cm.$^{-1}$	ε_A	4 A_1 νCC/νCN cm.$^{-1}$	ε_A	5 B_1 νCC/νCN cm.$^{-1}$	ε_A	6 — ?N$^+$–O$^-$ cm.$^{-1}$	ε_A
1	NH_2	2970	70	1640	190	1577	100	1548 / 1503	45 / 55	1449	80	—	
2	NHMe	2950	65	1628	230	1574	160	1533	145	1453	60	(—)	
3	NMe_2	2970	90	1618	230	1560	115	1510	220	1444 ‡	150	—	
4	OMe	2970	130	1613	105	1570	95	1503	200	1446	160	—	
5	OEt	2990	175	1617	175	1570	160	1504	290	1441	175	(—)	
6	NH·COMe	3000	90	1617	145	1572	280	1478	135	1428	350	(—)	
7	NH·COPh	2990	70	1612	140	1574	330	1482	200	1430	320	(—)	
8	NH·CO·Morph [b]	2990	140	1620	165	1577	370	1492 *	310	(—)		(—)	
9	NH·CO_2Et	3000	130	1620	140	1578	340	1487	175	1435	280	(—)	
10	NMe·COPh	3000	100	1610	90	1551	45	1500	280	1435	175	(—)	
11	Me	2970	110	1615	15	—		1491	105	1456	135	—	
12	CH_2·CH_2Ph	2970	100	(—)		—		1491 ‡	105	1441	170	1273 *	45
13	CH_2Ph	2970	85	(—)		—		1490 ‡	105	1437	185	1282	55
14	CH_2·C_6H_4·NO_2-*p*	2990	105	(—)		—		1490	145	1438	210	1282 *	60
15	CH:CHPh	2970	85	1610 ‡	50	1550	20	1484	95	1431	150	1303	45
16	Ph	2970	70	(—)		—		1478 ‡	130	1417	110	1295 *	20
17	C_6H_4·NO_2-*m*	2980	50	(—)		—		1471	60	1415	100	1290 *	35
18	S·CH_2Ph	3000	135	1594	35	1556	25	1471	220	1425	175	1270	125
19	Cl	3000	85	1602	5	—		1470	180	1427	150	1272	280
20	CH:CH·CO_2Et	2990	100	1610	25	—		1482	60	1431	185	(—)	
21	CN	3000	40	1602	15	—		1485	85	1430	240	1295	230
22	CO_2Et	2990	95	1610	30	1535	15	1483 *	25	1431	210	1270 *	155
23	CO_2Me	3010	90	1610	40	1537	15	1483	25	1430	200	1278 *	140
24	COMe	3000	80	1606	60	—		1479 *	10	1432	230	1284 *	60

No.	Subst.	7 — νN$^+$–O$^-$		8 ? ?		9 A_1 βCH		10 B_1 βCH		11 A_1 βCH		12 A_2 γCH	
		cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A
1	NH_2	($CHCl_3$)		1190	95	1152	20	1128	70	—		866	45
2	NHMe	($CHCl_3$)		1189	95	1157 ‡	150	1100	20	1039	10	839	40
3	NMe_2	($CHCl_3$)		1176 ‡	280	1143 ‡	95	1110	60	1055 ‡	60	839	160
4	OMe	($CHCl_3$)		1179	95	1153	30	1118	140	1052	45	843	80
5	OEt	($CHCl_3$)		1195 *	120	1156	35	1120 ‡	230	1052	40	836	120
6	NH·COMe	(1235	230)	1198 *	220	1150	35	1105	60	1040	30	853 / 821	45 / 95
7	NH·COPh	1260	245	1175 *	55	1150	25	1107	35	1040	20	863 / 810	70 / 20
8	NH·CO·Morph [b]	($CHCl_3$)		1175 *	80	1150	30	(—)		(—)		840	80
9	NH·CO_2Et	1252 ‡	530	1180 *	130	1150 *	140	1104	80	1040 ‡	100	854	75
10	NMe·COPh	1268	320	1174	60	1150	25	1122	90	1043	25	834	100
11	Me	1244	230	($CHCl_3$)		1150	10	1111	40	1049	25	851	185
12	CH_2·CH_2Ph	1245	185	1174	25	1142	35	1103	5	1048	15	877 / 847	20 / 60
13	CH_2Ph	1247	190	1175	55	1153	20	1100	10	1047	10	861	110
14	CH_2·C_6H_4·NO_2-*p*	1250	260	1180 *	95	1155	35	1112 ‡	80	1048	25	871 / 861 *	90 / 120
15	CH:CHPh	(1235	180)	1177	85	1150	40	1097	10	1045	15	856	80
16	Ph	1242	230	1185 *	40	1150	20	1111	30	1039	10	846	135
17	C_6H_4·NO_2-*m*	1245	230	(—)		1153	20	1113	30	1037	35	842	120
18	S·CH_2Ph	1248	150	($CHCl_3$)		1144	145	1092	95	1044	35	839	115
19	Cl	1257	200	1167	15	1145	190	1085	115	1042	25	849	145
20	CH:CH·CO_2Et	1268	250	(—)		1152	90	1110	25	1038	100	854 / 822	35 / 20
21	CN	1265	135	1190	70	1150	85	1100	5	1038	20	857	155
22	CO_2Et	1250	200	(—)		1150 *	110	1094 ‡	120	1044	50	853 / 831	30 / 20
23	CO_2Me	1255	200	1165 *	35	1151	75	1094 ‡	90	1045	50	856 / 815	110 / 10
24	COMe	1257	110	(—)		1148	50	1113	50	1042	50	851	110

[a] See footnote p. 2187 and also for meaning of other symbols. [b] Morpholide.

The second band (col. 5) occurs at 1456—1415 cm.$^{-1}$. Amines and ethers (Nos. 1—5) absorb at 1453—1441 cm.$^{-1}$, but amido-compounds (Nos. 6—10) at 1435—1428 cm.$^{-1}$, near the compounds with electron-attracting substituents (Nos. 21—24) at 1432—1430 cm.$^{-1}$. The band for the methyl compound is at 1456 cm.$^{-1}$, and for the methylene compounds (Nos. 12—14) at 1441—1437 cm.$^{-1}$; the position is lowered by attachment to a double



(I) (II) (III) (IV)

bond (Nos. 15, 20; at 1431 cm.$^{-1}$), a heavy atom (Nos. 18, 19; at 1427—1425 cm.$^{-1}$), and an aromatic ring (Nos. 16, 17; at 1417—1415 cm.$^{-1}$). The intensity is (60—350) [(185 ± 70)].

The 1300—1240 *cm.*$^{-1}$ *Region.*—The $^{+}N{-}O^{-}$ stretching band (col. 7) occurs at 1274—*ca.* 1220 cm.$^{-1}$. Compounds with weakly conjugating substituents (Nos. 11—14, 16—18) absorb at 1250—1242 cm.$^{-1}$; the frequency is raised by electron-acceptors (Nos. 21—24), and apparently lowered for the amines and ethers (Nos. 1—5). The position is variable for amido- (Nos. 6—10) and ethylenic compounds (Nos. 15 and 20), probably because of varying importance of interactions as in (I) and (II). The intensity is (110—320); [(210 ± 55)].

Compounds with saturated or electron-attracting substituents show a shoulder or subsidary band (col. 6) at higher frequencies than those of the main $^{+}N{-}O^{-}$ stretching band; in the chloro- and cyano-compounds it is stronger than the " main " band.

The 1200—1000 *cm.*$^{-1}$ *Region.*—Four bands are shown. The first (col. 8) is unobscured by solvent or substituent absorption in only nine compounds, 1190—1165 cm.$^{-1}$ (15—95) [1178 ± 8 cm.$^{-1}$ (65 ± 30)].

The second band (col. 9) is at 1157—1142 cm.$^{-1}$ [1150 ± 4]; the intensity is moderate for the chloro- and benzylthio-compounds (known to have nuclear bands strengthened in this region [6]) and where electron-accepting substituents are present (Nos. 20—24), but otherwise weak (10—40) [(25 ± 10)].

The third band (col. 10) is at 1128—1085 [1106 ± 10] cm.$^{-1}$; higher frequencies are found with electron-donating substituents (Nos. 1—10), and lower with heavy atoms (S, Cl). The intensity is (20—140) [(75 ± 35)] with electron-donating substituents, including chlorine and benzylthio (*i.e.*, Nos. 1—10, 18, 19), but in the other compounds (5—50) [(25 ± 20)].

The fourth band (col. 11), absent for the amino-compound, is otherwise at 1055—1037 [1044 ± 5] cm.$^{-1}$; the intensity is (10—50) [(25 ± 15)] (except in No. 19, strongly overlapped by a substituent band).

The 800 *cm.*$^{-1}$ *Region.*—All the compounds show one band at 866—834 cm.$^{-1}$ (30—185) [849 ± 9 cm.$^{-1}$ (95 ± 40)]. Often a subsidary band or shoulder is shown.

Assignments.—Comparison with Randle and Whiffen's data [7] on *ortho*-substituted benzene derivatives suggests the assignments at the head of the Table. Nothing corresponding to the bands from these benzene derivatives at [1315 ± 11 (m), 977 ± 9 (w), 934 ± 11 (w) cm.$^{-1}$] was found, and the band in col. 8 does not correspond to a band in these compounds, but otherwise agreement is quite good (means usually within 15 wave numbers). Absorption analogous to that below 800 cm.$^{-1}$ in *ortho*-substituted benzene derivatives would be obscured by the solvent in our work.[4]

[6] Katritzky *et al.*, preceding and following papers and unpublished work.
[7] Randle and Whiffen, Paper No. 12, Conference on Molecular Spectroscopy, 1954, Institute of petroleum, p. 111.

This work supports our conclusions [8] that 2-methylamino- and 2-amino-pyridine 1-oxide exist as (III) and not in the imino-forms (IV) and indicates that acylamino-compounds behave similarly.

Experimental.—See ref. 1 for sources of specimens and measurements of spectra.

THE DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, January 21st,* 1958.]

[8] Gardner and Katritzky, *J.*, 1957, 4375.

---

447. *Infrared Studies of Heterocyclic Compounds. Part I. 4-Substituted Pyridines.*

By A. R. KATRITZKY and J. N. GARDNER.

4-Monosubstituted pyridines show eight characteristic bands in chloroform; their positions and intensities are recorded and discussed for forty-eight compounds.

AVAILABLE information about the infrared spectra of heterocyclic compounds is very much less than their importance justifies. Thus in the two reviews by Bellamy [1] and by Jones and Sandorfy [2] only *ca.* 3% of the space is devoted to the topic. We considered that it was of interest to compare a large number of spectra, measured under standard conditions, in which only one parameter was being changed; after our work [3] on substituted pyridine 1-oxides this paper is devoted to the spectra of forty-eight 4-monosubstituted pyridines. Of the bands with $\varepsilon_A \geqslant 15$, eight were found to be characteristic of the nucleus and are recorded in the Table; the other bands were, with few exceptions, characteristic of the substituent. For reasons given previously [4] the spectra were all measured at 0·2M-concentration in chloroform in a 0·117 mm. cell, and apparent molecular extinction coefficients recorded.

The detailed spectrum of 4-picoline as liquid and gas is known.[5] Cook and Church [6] investigated the spectra of 4-benzyl- and six 4-alkyl-pyridines as liquid films, and recorded the positions of characteristic bands, without giving any intensities. The bands at 1613—1597, 1570—1555, 1508—1490, 1422—1406, 1072—1067, 1000—995, and 822—785 cm.$^{-1}$ which they record correspond to those discussed in this paper. They also record absorption near 1460 and 1380 cm.$^{-1}$ which may be assigned to substituent CH deformation; near 1230 cm.$^{-1}$, which would be obscured by solvent absorption in our work; and near 1300 cm.$^{-1}$ which we have not found: the last band was stated to be " of variable intensity " and assigned to an overtone. The actual positions of the bands found in the two investigations show fair agreement considering the difference in state; our compounds with a saturated carbon atom directly attached to the ring usually show a smaller range than that reported by Cook and Church: [6] *e.g.*, in the liquid, 4-picoline absorbs at 1406 cm.$^{-1}$, and 4-ethylpyridine at 1422 cm.$^{-1}$, but in chloroform solution both absorb at 1415 cm.$^{-1}$. Shindo and Ikekawa [7] discussed certain portions of the spectra of the 4-methyl and 4-ethyl compounds, in connexion with a general investigation into alkylpyridines, and the spectra of the 4-chloro-, 4-methoxy-, and 4-nitro-compound have also been recorded.[8]

The 3000 *cm.*$^{-1}$ *Region.*—Usually only one band is resolved, and for reasons discussed

[1] Bellamy, " The Infrared Spectra of Complex Molecules," Methuen, London, 1956.
[2] Jones and Sandorfy in Weissberger, " Technique of Organic Chemistry, Vol. IX. Chemical Applications of Spectroscopy," Interscience, London, 1956.
[3] Katritzky and Gardner, *J.*, 1958, 2192; Katritzky and Hands, *J.*, 1958, 2195.
[4] Katritzky, Monro, Beard, Dearnaley, and Earl, *J.*, 1958, 2182.
[5] Long, Murfin, Hales, and Kynaston, *Trans. Faraday Soc.*, 1957, **53**, 1171.
[6] Cook and Church, *J. Phys. Chem.*, 1957, **61**, 458.
[7] Shindo and Ikekawa, *Pharm. Bull.* (*Japan*), 1956, **4**, 192.
[8] Costa and Blasina, *Z. phys. Chem.* (*Frankfurt*), 1955, **4**, 24.

XUM

		1		2		3		4	
		$CHCl_3$		A_g		B_{1g}		B_{2u}	
		νCH		νCC, νCN		νCC, νCN		νCC, νCN	
No.	Subst.	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A
1	NMe_2	2940	110	1607	560	1550 *	80	1522	170
2	NHPh	2940	35	1595	430	1560	40	1510	185
3	NH_2	2930	55	1606	290	1573	45	1503	50
4	OMe	2960	75	1601	430	1576	155	1505	200
5	OEt	2980	90	1600	320	1570	100	1501	130
6	NH·COMe [a]	2940	55	1590	390	1570 *	30	(—)	
7	NH·COPh [a]	2960	50	1593	300	(—)		(—)	
8	Me [b]	2970	55	1610	135	1565	15	1499	15
9	Et	2970	70	1606	125	1561	15	1493	10
10	CH_2·CH_2Ph	2960	75	1608	180	1563	20	(—)	
11	CH_2·CH_2·NH·CO·CH_2Ph	2960	95	1610	185	1560 *	60	(—)	
12	CH_2·CH_2·NH·COPh	2970	75	1608	165	(—)		(—)	
13	CH_2·CH_2·NHTs [c]	2950	55	1609	145	1565	15	(—)	
14	CH_2·CH_2·CO_2Me	2960	85	1608	165	1560	25	1490	10
15	CH_2·CH_2·CO_2Et	2970	80	1609	160	1563	30	—	
16	CH_2Ph	2960	50	1602	180	1560	15	(—)	
17	CH_2·C_6H_4·NO_2-*p*	2960	35	1601	130	1563	25	(—)	
18	CH_2·CS·NH·CH_2·CH_2Ph	2980	85	1608	120	1565 *	25	1500 *	80
19	CH_2·CS·Pip [d]	2950	165	1601	190	1560	15	(—)	
20	CH_2·CS·Morph [e]	2980	115	1601	170	1560	15	(—)	
21	CH_2·COPh	2980	70	1608	175	1566	35	(—)	
22	CH_2·CO_2Me	2970	80	1610	135	1566	25	1496	10
23	CH_2·CO_2Et	2990	75	1608	115	1568	25	—	
24	CH_2·CO·NH·CH_2Ph	2970	70	1603	180	1558 *	50	(—)	
25	CH_2·CO·NHPh	2950	55	1602 ‡	260	(—)		(—)	
26	CH(CH_2Ph)(CO·Morph) [e]	2980	90	1600	185	1560	20	(—)	
27	C:CPh	2990	50	1600	220	1540 *	15	(—)	
28	C:C·C_6H_4·NO_2-*p*	2980	65	1601 ‡	400	(—)		(—)	
29	CH:CHPh	2970	50	1600	290	1552	15	(—)	
30	CH:CH·C_6H_4Cl-*p*	2980	70	1603 ‡	260	1553	15	(—)	
31	CH:CH·C_6H_4·NO_2-*p*	2980	70	1601 ‡	380	1553 *	30	(—)	
32	C(CHPh)(CO·Morph)	2980	110	1600	350	1545	35	(—)	
33	CH:CH·CO_2Me	2960	65	1600	170	1550	65	1492	15
34	CH:CH·CO_2Et	2970	70	1601	165	1549	35	1496	10
35	Ph	2950	50	1596	130	1546	20	(—)	
36	C_6H_4·NO_2-*p*	2970	40	1606	105	1551 ‡	105	(—)	
37	CH_2·OH	2960	60	1610	90	1564	25	—	
38	CHPh·OH	2980	55	1602	115	1562	25	(—)	
39	CMe(CN)·OAc	2990	40	1604	120	1568	20	—	
40	CMe(CN)·OBz	2980	45	1600	165	1567	20	(—)	
41	CMe:N·NH_2	2980	45	1590	135	1545	10	—	
42	Cl	2980	35	1575	280	1565 *	115	1482	100
43	CN	2990	30	1600	90	1558	30	1490	10
44	CO_2Me	2970	60	1604	45	1565	40	1490	10
45	CO_2Et	2990	85	1602	35	1567	45	1490	5
46	CHO	2990	30	1600	15	1572	75	1490	15
47	COMe	2980	35	1600	35	1555	30	1489	15
48	NO_2	2990	20	1604	25	1575	65	1480 *	15

See footnote, p. 2192, and also for meaning of other symbols.

[a] Measured at 0·02M-concentration in 1 mm. cell because of poor solubility. [b] Measured at 0·4M-concentration. [c] Toulene-*p*-sulphonyl derivative. [d] Piperide. [e] Morpholide.

in ref. 3 this is assigned mainly to the CH stretching of the solvent, displaced by hydrogen bonding with the pyridine. The band occurs at 2990—2930 [2970 ± 15] cm.$^{-1}$; * electron attracting substituents tend to raise the frequency (cf. expected weaker H-bond formation). Compounds with weakly conjugating substituents (Nos. 8—41, except 19, 20, 26, and 32 where there is serious overlapping by substituent absorption) have intensity (35—95) [(65 ± 15)]; * when electron-withdrawing substituents are present (Nos. 42—48) this intensity is (20—35) (except for the esters). Consideration of Nos. 1—7 is complicated

* For the significance of parentheses and brackets see *J.*, 1958, p. 2187.

		5		6		7		8	
		B_{2u}		?		A_u, B_{2g}		B_{1u}	
		$\begin{cases}\nu CC\\ \nu CN\end{cases}$		βCH		γCH		γCH	
No.	Subst.	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A
1	NMe_2	(—)		(—)		991	300	805	105
2	NHPh	1412	30	(—)		992	105	807	50
3	NH_2	1432	25	—		991	140	815	120
4	OMe	1425	60	—		992	65	819	190
5	OEt	1415	25	—		993	95	809	105
6	NH·COMe [a]	($CHCl_3$)		—		996	80	($CHCl_3$)	
7	NH·COPh [a]	($CHCl_3$)		1072 ‡	55	994	50	($CHCl_3$)	
8	Me [b]	1415	35	1068	15	997	45	—	
9	Et	1415	40	1065	10	996	30	819	60
10	CH_2·CH_2Ph	1418	50	1070 *	20	996	45	805	55
11	CH_2·CH_2·NH·CO·CH_2Ph	1416	100	1068	25	994	45	—	
12	CH_2·CH_2·NH·COPh	1418	65	1068	35	995	45	—	
13	CH_2·CH_2·NHTs [a]	1418	125	1070 *	110	994	25	814	110
14	CH_2·CH_2·CO_2Me	1418	80	1068	20	992	35	—	
15	CH_2·CH_2·CO_2Et	1416	75	1071	25	997	40	808	40
16	CH_2Ph	1418	65	1069	30	996	40	825	20
17	CH_2·C_6H_4·NO_2-*p*	1418	45	1070	20	997	20	825	10
18	CH_2·CS·NH·CH_2·CH_2Ph	1418	140	1070	35	993	20	—	
19	CH_2·CS·Pip [d]	1418	90	1070	30	995	40	—	
20	CH_2·CS·Morph [a]	1418 *	120	1069 *	50	995	35	—	
21	CH_2·COPh	1419	65	1071 ‡	30	995 *	90	—	
22	CH_2·CO_2Me	1419	80	1071	25	996	50	—	
23	CH_2·CO_2Et	1419	70	1071	25	997	30	—	
24	CH_2·CO·NH·CH_2Ph	1418	80	1070	30	994	30	—	
25	CH_2·CO·NHPh	1419	80	1070	15	995	15	—	
26	CH(CH$_2$Ph)(CO·Morph) [a]	1416 *	125	1068 ‡	70	993	35	—	
27	C≡CPh	1410	45	1068	15	990	45	820	120
28	C≡C·C_6H_4·NO_2-*p*	1409	70	1066	10	990	35	819	155
29	CH:CHPh	1415	30	1068	10	994	65	802	50
30	CH:CH·C_6H_4Cl-*p*	1417	45	1065	10	992	55	(—)	
31	CH:CH·C_6H_4·NO_2-*p*	1417	60	1065	10	991	50	—	
32	C(CHPh)(CO·Morph) [a]	1415	135	1070 ‡	65	995 *	50	813	60
33	CH:CH·CO_2Me	1414	85	1066	10	990	65	812	140
34	CH:CH·CO_2Et	1415	80	1067	15	992	55	813	120
35	Ph	1409	50	1068	20	990	25	827	80
36	C_6H_4·NO_2-*p*	1413	30	1070	15	993	30	817	190
37	CH_2·OH	1416	85	(—)		994	45	—	
38	CHPh·OH	1414	95	1066 *	30	994	40	—	
39	CMe(CN)·OAc	1416	105	(—)		996	35	818	120
40	CMe(CN)·OBz	1415	100	(—)		995	35	818	135
41	CMe:N·NH_2	1410	55	1061	30	993	45	820	90
42	Cl	1409	110	1062	40	985	10	809	110
43	CN	1412	100	1069	20	993	30	819	150
44	CO_2Me	1411	130	1065	80	995	45	829	15
45	CO_2Et	1412	105	1066	100	994	30	—	
46	CHO	1416	85	1060	20	992	25	(803	55)
47	COMe	1411	120	1064	40	993	25	813	115
48	NO_2	1405	65	1055	30	992	30	—	

by two compounds' being measured at 0·02M-concentration, and the possibility of intramolecular hydrogen-bonding.

The 1650—1550 *cm.*$^{-1}$ *Region.*—Two bands occur. The stronger (col. 2) occurs at 1610—1590 [1603 ± 5] cm.$^{-1}$ except for the chloro-compound (No. 42); halogens are known [3] to lower this band's frequency in other cases. The intensity depends on the electron-donor properties of the substituent. For amino-, amido-, alkoxy-, and chloro-substituents, it is ⩾280; for strongly electron-withdrawing substituents (Nos. 44—48) it is ⩽45. For groups with relatively weak electronic effects (Nos. 8—41) the intensity is (90—290) [(155 ± 40)] (except for No. 32 where there is strong overlapping by the carbonyl group). Phenyl groups, of course, also absorb in this region, but much less

strongly;[9] however, it is possible to discern their influence. Assignment of this and the other bands is discussed at the end of the paper.

The second band in this region is usually much weaker. When the ring is attached to a saturated carbon atom (Nos. 8—26 and 37—40), position and intensity are fairly constant at 1568—1560 cm.$^{-1}$ (15—35) [1563 ± 3 cm.$^{-1}$ (20 ± 5)]. Strongly electron-donor substituents (Nos. 1—7) tend to raise both frequency and intensity (cf. the corresponding band in benzenes[10]). Carbon–carbon multiple bonds (Nos. 27—36) lower the frequency to 1553—1545 cm.$^{-1}$. Electron-acceptors (Nos. 43—48) tend to raise the intensity, but the position varies from 1575 to 1555 cm.$^{-1}$.

The 1500—1400 *cm.*$^{-1}$ *Region.*—A band (col. 4) frequently occurs at 1522—1480 cm.$^{-1}$; compounds with powerful electron-donor substituents (Nos. 1—5) absorb strongly at above 1500 cm.$^{-1}$, whereas those with electron-accepting substituents (Nos. 43—48) absorb weakly at 1490 cm.$^{-1}$ or below. Chlorine behaves as an electron-donor as regards the intensity, but as acceptor as regards the position of the band. The band is masked in amides and compounds with phenyl groups by substituent absorption; of the remaining compounds with weakly conjugating substituents, weak absorption is shown at 1500—1490 cm.$^{-1}$ in seven, and for five others the band is absent or too weak to be recorded.

All the compounds show a second band in this region (col. 5) at 1432—1405 [1415 ± 4] cm.$^{-1}$. Only the amino- and methoxy-compounds absorb above 1419 cm.$^{-1}$; all the nineteen compounds (Nos. 8—25, 37) in which the ring is directly attached to a CH_2 group absorb at 1419—1415 cm.$^{-1}$; carbon–carbon triple bonds and strongly electron-withdrawing substituents tend to lower the frequency to *ca.* 1411 cm.$^{-1}$. The intensity of this band is especially affected by overlap with substituent bands for Nos. 13, 18—20, 26, and 32; otherwise it is (25—130) [70 ± 25] with a definite tendency to be raised by electron-accepting substituents.

The 1080—980 *cm.*$^{-1}$ *Region.*—Two bands are in general found. The first (col. 6) at 1072—1055 [1067 ± 3·5] cm.$^{-1}$ is not found for compounds with strongly electron-donor substituents (Nos. 1—6); with weakly conjugating substituents (Nos. 8—40) the band is in the narrower range 1071—1065 cm.$^{-1}$ with intensity (10—35) [(20 ± 8)]; electron-attracting groups (Nos. 41—48) tend to lower the frequency, and increase the intensity.

All the compounds show a band at 997—985 [993 ± 2·5] cm.$^{-1}$ (Col. 7). The intensity is high with strongly electron-donor substituents (Nos. 1—7); otherwise it is (10—50) [(35 ± 10)], except for compounds where CH:CH-deformation absorption overlaps (Nos. 29—34).

The 800 *cm.*$^{-1}$ *Region.*—Many of the compounds show a band at just above 800 cm.$^{-1}$. This is probably a ring CH deformation frequency,[7] present for the remaining compounds below 805 cm.$^{-1}$, where it is obscured by solvent absorption.

Assignments.—Comparison with Randle and Whiffen's data[11] for *para*-substituted benzenes suggests the tentative assignments indicated at the head of the Table. There can be little doubt about those in cols. 2, 3, 4, and 5, where the corresponding *para*-benzene absorption is at [1620 ± 8, 1571 ± 11, 1512 ± 12, and 1450 ± 10 cm.$^{-1}$] with average intensities of m, w, vs, and m. Col. 6 probably records an in-plane CH deformation, corresponding to one of two *para*-benzene frequencies B_{3u} or B_{2u} at respectively [1125 ± 10 and 1018 ± 10 cm.$^{-1}$]. The corresponding *para*-benzenoid absorption for the two CH out-of-plane deformation modes (cols. 7, 8) is at [961 ± 12, 817 ± 13 cm.$^{-1}$].*

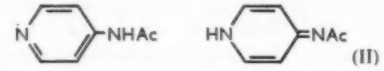
* [*Added* 28.1.1958.] A Referee has commented that, whereas for vibrations of predominately CH character the 4-substituted pyridines are correctly compared with *para*-disubstituted benzenes, for skeletal vibrations, comparison should be with monosubstituted benzenes (i.e., that, from the point of view of the ring, an electron pair is more like a hydrogen atom than a heavier substituent). As the Referee points out, this would not affect the assignments in cols. 2—5, for here the pattern of absorption is similar in both mono- and *para*-di-substituted benzenes,[11] but it suggests an alternative assignment of col. 7 to a vibration corresponding to the A_1 ring vibration at [1001 ± 4 cm.$^{-1}$] in monosubstituted benzenes.[11]

[9] Katritzky and Lagowski, unpublished results.

[10] Ref. 1, p. 61.

[11] Randle and Whiffen, Report on Conference on Molecular Spectroscopy, 1954, Institute of Petroleum, Paper No. 12.

The above work indicates that 4-acetamido- and 4-benzamido-pyridine exist as such (as I) and not in the alternative forms (as II). Other evidence that this is so will be published separately.



(I) (II)

Experimental.—The preparation of most of the compounds has already been described.[3, 4, 12] Specimens were recrystallised or redistilled immediately before measurement.

A Perkin-Elmer model 21 instrument was used with a sodium chloride prism, slit programme 4, and the settings previously given.[4]

THE DYSON PERRINS LABORATORY, THE UNIVERSITY, OXFORD. [*Received, January 14th*, 1958.]

[12] See also Katritzky and his co-workers, *J.*, 1955, 2581, 2587; 1956, 2063, 2404; 1957, 191, 1769, 4375; 1958, 150, 1263.

---

448. *Infrared Studies of Heterocyclic Compounds. Part II.*[1] *2-Monosubstituted Pyridines.*

By A. R. KATRITZKY and A. R. HANDS.

The positions and intensities of ten characteristic bands are recorded and discussed for thirty-five 2-substituted pyridines.

AFTER our work [1] on 4-substituted pyridines, we now report on some 2-analogues. 2-Picoline has been studied in detail,[2] but the only previous comparative work was that by Cook and Church [3] on 2-benzyl- and five 2-alkyl-pyridines; bands were reported at 1603—1597, 1577—1575, 1477—1474, 1468—1437, 1311—1299, 1152—1146, 1052—1050, and 995 cm.$^{-1}$ corresponding to those now discussed, except that at *ca.* 1093 cm.$^{-1}$. Bands noted [3] at 1225 and 750—743 cm.$^{-1}$ are obscured by solvent in our work; other absorption found [3] has been shown [4] due to the substituent: *e.g.*, that at 1501 and 1458 cm.$^{-1}$ is due to the benzene ring in 2-benzylpyridine.

The 3000 *cm.*$^{-1}$ *Region.*—The hydrogen-bonded chloroform CH stretching frequency [1] occurs at 3000—2940 cm.$^{-1}$ (10—100) [2980 $\pm$ 15 cm.$^{-1}$ (50 $\pm$ 25)].*

The 1650—1550 *cm.*$^{-1}$ *Region.*—Two bands occur. The first (col. 2 of the Table) is at 1616—1573 cm.$^{-1}$, but only strong electron-donor substituents cause absorption above 1600 cm.$^{-1}$. When the ring is attached to a saturated carbon atom (Nos. 10—14, 23—24) the band is at 1600—1595 cm.$^{-1}$; the frequency is lowered by carbon–carbon multiple bonds (Nos. 15—22 at 1593—1585 cm.$^{-1}$), electron-accepting substituents (Nos. 27—35 at 1590—1585 cm.$^{-1}$), and heavy atoms (Cl and Br; Nos. 25, 26; at 1586—1573 cm.$^{-1}$). Intensities tend to decrease from electron-donor to electron-acceptor substituents; they are (100—290) [(170 $\pm$ 65)] in Nos. 1—9 (65—150) [115 $\pm$ 25)] in Nos. 10—26 (except Nos. 18, 19, and 22 strongly overlapped by substituent absorption), and (50—100) [(75 $\pm$ 20)] with electron-withdrawing substituents (Nos. 27—34; the nitro-compound is lower still).

The second band (col. 3) is at 1581—1562 [1572 $\pm$ 4] cm.$^{-1}$. Intensity variation is similar to that for the previous band: (80—235) [(160 $\pm$ 55)] for Nos. 1—9; (30—75) [(50 $\pm$ 10)] for Nos. 10—24 (except Nos. 18, 19, 21, and 22 overlapped); and (25—45) [(35 $\pm$ 10)] for Nos. 27—35.

* Arithmetical means and standard deviations: see footnote, *J.*, 1958, 2182.

[1] Part I, Katritzky and Gardner, preceding paper.
[2] Long, Murfin, Hales, and Kynaston, *Trans. Faraday Soc.*, 1957, **53**, 1171, and references therein.
[3] Cook and Church, *J. Phys. Chem.*, 1957, **61**, 458.
[4] Katritzky *et al.*, preceding papers and unpublished work.

The 1500—1400 *cm.*$^{-1}$ *Region.*—Two bands are found. One (col. 4) is at 1483—1460 [1471 ± 6] cm.$^{-1}$ except in the halogeno-compounds where it is considerably lower (cf. other cases [4]). Intensities are (140—340) with the strongest electron-donors (Nos 1—4), (10—35) with stronger electron-acceptors (Nos. 29—35), and for the rest (30—125) [(80 ± 25)].

The other band is at 1443—1420 [1433 ± 5] cm.$^{-1}$ except in the bromo-compound at 1414 cm.$^{-1}$ (cf above). Electron-donor substituents (Nos. 1—9), and especially amido-compounds with adjacent NH (Nos. 6—9), raise the intensity, which otherwise (Nos. 10—35) is (20—145) [(70 ± 30)].

The 1300—1240 *cm.*$^{-1}$ *Region.*—Nine compounds absorb weakly at 1293—1250 cm.$^{-1}$ (10—35); for others there is a shoulder hereabouts.

The 1200—990 *cm.*$^{-1}$ *Region.*—Four bands are found. The first (col. 7) is at 1152—1140 [1147 ± 3] cm.$^{-1}$. Electron-donor substituents (Nos. 1—9) give intensities of (35—80) [(60 ± 15)], acceptor substituents (Nos. 27—35) give intensities of (5—25) [(15 ± 5)], and the remainder (Nos. 10—26) intensities of (10—50) [(25 ± 10)].

Another band (col. 8) is at 1102—1083 cm.$^{-1}$ (5—70) [1093 ± 4 cm.$^{-1}$ (15 ± 15)] except for the halogeno-compounds (Nos. 25, 26) which both show two strong bands hereabouts (cf. other cases [4]).

A third band is at 1059—1039 [1048 ± 5] cm.$^{-1}$. Its intensity is (5—50) [(20 ± 10)], except for Nos. 9 and 23 (strongly overlapped by substituent-absorption) and for the esters (Nos. 29 and 30).

		1 [a]		2		3		4		5	
		$CHCl_3$		A_1		B_1		A_1		B_1	
		νCH		νCC / νCN		νCC / νCN		νCC / νCN		νCC / νCN	
No.	Subst.	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A
1	NH_2	2960	40	1616 ‡	460	1574	115	1483	220	1443	240
2	OMe	3000	65	1610 / 1590 *	165 / 95	1578	150	1483	340	1420	185
3	OEt	2990	100	1600	180	1574	125	1470	240	1433	250
4	O·CH_2Ph	3000	40	1601	125	1573	80	1475	140	1433	155
5	NMe·COPh	3000	80	1592	230	1573	165	1472 ‡	260	1442	160
6	NH·COMe	2980	50	1600	120	1580	220	1460	60	1434	325
7	NH·COPh	3000	35	1601	140	1581	200	(—)		1434	335
8	NH·CO·Morph [b]	2980	90	1599	100	1580	235	(—)		1432 ‡	380
9	NH·CO_2Et	2980	95	1593	290	(—)		1480 *	45	1443	330
10	Me	2960	65	1595	70	1571	40	1478	85	1430	40
11	Et	2950	90	1595	110	1570	45	1476	85	1431	60
12	CH_2·CH_2Ph	2950	60	1598	125	1574	45	1478	85	1436	75
13	CH_2Ph	2940	35	1596	130	1571	50	1473	75	1432 ‡	80
14	CH_2·C_6H_4·NO_2-*p*	2940	45	1590	140	1571	75	1472	70	1432	80
15	C:CPh	2970	40	1585	150	1563	45	1463	125	1428	60
16	CH:CHPh	2970	50	1592 ‡	180	1566	55	1471	110	1431	60
17	CH:CH·CO_2Et	2990	75	1587	85	1570	45	1468	80	1432	100
18	C_6H_4·NH_2-*p*	2980	40	1598	190	1570	80	1471 ‡	220	1428 *	40
19	C_6H_4·NH_2-*m*	2980	50	1595	195	1570	105	1478 *	70	1424	60
20	Ph	2970	50	1592	105	1568	45	1470 ‡	130	1427	60
21	C_6H_4·NO_2-*m*	2950	35	1593	130	1575	70	1473	70	1431 *	85
22	C_6H_4·NO_2-*p*	2990	30	1591	170	1573	90	1468	115	1438	85
23	CH_2·OH	2950	25	1600	65	1573	30	1476	30	1439	40
24	CHPh·OH	3000	20	1599	90	1577	50	1473	45	1438	85
25	Cl	2980	30	1586	130	1562 *	55	1451	95	1420	110
26	Br	2980	40	1573	115	1562	145	1444	115	1414	145
27	CH:N·OH	2970	60	1590	80	1571	45	1475	55	1436	50
28	CN	3000	20	1585	90	(—)		1462	65	1431	65
29	CO_2Me	3000	90	1590	50	1575	35	1470	30	1433	115
30	CO_2Et	2980	95	1590	70	1572	40	1465 ‡	55	1438	80
31	CHO	2980	30	1590	75	1578 *	20	1470	10	1438	20
32	COMe	2980	35	1586	55	1571	25	1467	20	1436	45
33	CO·C_6H_4·NO_2-*m*	2990	20	1588	90	(—)		(—)		1436	55
34	CO·C_6H_4·NO_2-*p*	2990	10	1588	100	1560 *	35	1468	15	1434	30
35	NO_2	3000	20	1595 *	10	1567 *	50	1460	35	1430	80

[a] See footnote, p. 2192, and also for meaning of other symbols. [b] Morpholide.

		6 A_1 ?		7 A_1 βCH		8 B_1 βCH		9 A_1 βCH		10 A_2 γCH	
No.	Subst.	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A
1	NH_2	1270 *	35	1149	70	—		1043	20	990	35
2	OMe	1270 *	115	1141	70	1097	10	1045 ‡	110	987	50
3	OEt	(—)		1140	80	(—)		(—)		988	40
4	O·CH_2Ph	(—)		1140	35	1090 *	50	1040	40	988	60
5	NMe·COPh	(—)		1150	35	1094 *	30	1051	40	993	25
6	NH·COMe	1280 *	25	1149	60	1092	10	1050	20	1000	30
7	NH·COPh	(—)		1149	60	1093	45	1049	20	992	25
8	NH·CO·Morph [5]	1265 *	115	1148	65	(—)		1047	25	986	65
9	NH·CO_2Et	1282 *	120	1152	75	1098 *	85	1050	70	995	40
10	Me	1293	35	1147	30	1099	10	1049	30	999	20
11	Et	—		1146	30	1102	5	1047	25	995	30
12	CH_2·CH_2Ph	1258 *	15	1149	10	—		1051	10	996	15
13	CH_2Ph	1270 *	10	1146	10	1091	10	1050	10	997	30
14	CH_2·C_6H_4·NO_2-*p*	(—)		1144	15	(—)		1048	20	996	35
15	C:CPh	1285	15	1145	25	1090	10	1042	10	990	30
16	CH:CHPh	—		1148	50	1092	5	1048	10	992	30
17	CH:CH·CO_2Et	(—)		1148 *	105	1092 ‡	55	1038 *	90	993	55
18	C_6H_4·NH_2-*p*	1267 *	90	1152	25	1095	10	1059	10	990	20
19	C_6H_4·NH_2-*m*	1274	15	1151	35	1094	20	1059	10	992	40
20	Ph	1292	10	1150	20	1094	10	1059 *	5	998	15
21	C_6H_4·NO_2-*m*	(—)		1144	15	(—)		1050	20	997	30
22	C_6H_4·NO_2-*p*	1270	10	1151	30	1097	35	1059	5	991	20
23	CH_2·OH	—		1145	20	1095	10	1053	70	996	20
24	CHPh·OH	—		1149	30	1098 *	15	1051 *	70	1000	30
25	Cl	1282	20	1147	50	1121 1083	190 75	1044	35	991	45
26	Br	1280	15	1144	25	1108 1076	215 145	1040	50	989	55
27	CH:N·OH	(—)		1149	25	1093	20	1048	10	995 *	90
28	CN	1281	10	1150	15	1090	15	1044	25	992	60
29	CO_2Me	1282 *	140	(—)		1089 ‡	45	1046	65	998	55
30	CO_2Et	1282 *	180	(—)		(—)		1045	90	995	100
31	CHO	(—)		1149	10	1088	15	1040	20	994	50
32	COMe	(—)		1146	15	1100	70	1043	35	996	30
33	CO·C_6H_4·NO_2-*m*	1274 *	85	1150	15	(—)		1046	20	997	115
34	CO·C_6H_4·NO_2-*p*	(—)		(—)		1090	30	1044	10	997	95
35	NO_2	1250	20	1145	5	1083	10	1039	30	996	65

The final band in this region (col. 10) is at 1000—986 cm.$^{-1}$ (15—115) [1094 ± 4 (45 ± 25)] cm.$^{-1}$.

Assignments.—Comparison with Randle and Whiffen's data [5] for *ortho*-substituted benzene derivatives suggests the assignments indicated at the head of the Table. The means are usually within 20 cm.$^{-1}$ and all our bands are accounted for; of the bands reported for the benzene derivatives, only those at [934 ± 11 (w) and 865 ± 14 (w)] cm.$^{-1}$ have no analogues.

Experimental.—See Part I [1] for sources of specimens and measurement of spectra.

THE DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, January 27th*, 1958.]

[5] Randle and Whiffen, Paper No. 12, Report on Conference of Molecular Spectroscopy, 1954, Institute of Petroleum, p. 111.

449. *Reactions of Unsaturated Compounds. Part XIV.* The Oxidation of 2 : 2 : 4 : 6 : 6-Pentamethylhept-3-ene.*

By M. A. Davis and W. J. Hickinbottom.

2 : 2 : 4 : 6 : 6-Pentamethylhept-3-ene is oxidised by chromic acid in aqueous sulphuric acid to 2-*tert.*-butyl-2 : 4 : 4-trimethylpentanoic acid together with the normal products of oxidative fission. 2 : 2 : 4-Trimethylhex-1-ene and 2 : 2-dimethyl-4-ethylhex-3-ene similarly give tertiary carboxylic acids by oxidative rearrangement, although in relatively low yield.

The significance of these results is discussed in the light of other observations.

It has been shown [1,2] that the products of the oxidation of an olefin by chromic acid in aqueous sulphuric acid can be predicted qualitatively from a knowledge of the behaviour of the epoxide towards aqueous sulphuric acid. Striking examples of this are the formation of *tert.*-butyl methyl ketone (II*a*) from 2 : 3-dimethylbut-2-ene [1] (I*a*), of 2 : 2 : 3 : 3-tetramethylbutanoic acid (III*a*) from 2 : 2 : 4-trimethylpent-2-ene [3] (I*b*), and of 2 : 2 : 3-trimethylbutanoic acid (III*b*) from 2 : 4-dimethylpent-2-ene [2] (I*c*).

	RR′C:CR″R‴ (I)					RR′R″C·COR‴ (II)					RR″R‴C·CO_2H (III)		
	R	R′	R″	R‴		R	R″	R‴					
I*a* and II*a*	Me	Me	Me	Me	III*a*	Bu^t	Me	Me					
I*b*	Bu^t	H	Me	Me	III*b*	Pr^i	Me	Me					
I*c*	Pr^i	H	Me	Me	III*c*	Bu^t	Me	Et					
I*d*	Bu^t	H	Me	Et	III*d*	Bu^t	Et	Et					
I*e*	Bu^t	H	Et	Et	III*e*	Bu^t	Me	CH_2Bu^t					
I*f*	Bu^t	H	Me	CH_2Bu^t									

This paper records the results of an extension of the examination to three trisubstituted olefins (I*d*, *e*, and *f*) to test the view that oxidation by chromic acid is dependent on the intermediate formation of an epoxide or its conjugate acid.

Oxidation of 2 : 2 : 4 : 6 : 6-pentamethylhept-3-ene (I*f*) by chromic acid in aqueous sulphuric acid gives a good yield of a tertiary carboxylic acid (III*e*) together with 2 : 2-dimethylpropanoic acid and methyl *neo*pentyl ketone, the normal products of oxidative fission. There is also formed a carbonyl compound having constants very close to those reported by Miner [4] for a compound isolated on oxidation of technical tri*iso*butylene, a mixture mainly of 2 : 2 : 4 : 6 : 6-pentamethylhept-3-ene and 4 : 4-dimethyl-2-*neo*pentylpent-1-ene. It is probable that Miner's carbonyl compound and ours are identical and this view is supported by the close agreement between the melting point of the oximes and 2 : 4-dinitrophenylhydrazones. Miner considered his compound to be 2 : 2 : 4 : 6 : 6-pentamethylheptane-3 : 5-dione. The substance we obtained has none of the properties of a 1 : 3-diketone and we suggest that it is 4-hydroxy-2 : 2 : 4 : 6 : 6-pentamethylheptan-3-one. The formation of such a compound is not unexpected and is in keeping with observations in the steroid series (cf. Fieser [5]).

The oxidation of 2 : 2 : 4-trimethylhex-3-ene (I*d*) and of 4-ethyl-2 : 2-dimethylhex-3-ene (I*e*) by chromic acid in aqueous sulphuric acid also gives the tertiary carboxylic acids (III*d*) and (III*c*) respectively, although in much lower yield than in the case of 2 : 2 : 4 : 6 : 6-pentamethylhept-3-ene. The main products are 2 : 2-dimethylpropanoic acid and ketones derived by oxidative fission. The neutral products of the oxidation of each olefin are

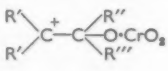
* Part XIII, *J.*, 1957, 4195.

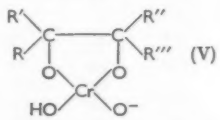
[1] Hickinbottom, Hogg, Peters, and Wood, *J.*, 1954, 4400.
[2] Hickinbottom, Peters, and Wood, *J.*, 1955, 1360.
[3] Byers and Hickinbottom, *J.*, 1948, 1334.
[4] Miner, Ph.D. Thesis, Penn. State College, Univ. Microfilms no. 260.
[5] Fieser, *J. Amer. Chem. Soc.*, 1953, **75**, 4386.

XUM

however more complex than can be accounted for on the basis of normal oxidative fission. Thus, from 2 : 2 : 4-trimethylhex-3-ene (I*d*) 3 : 5 : 5-trimethylhexan-2-one is obtained together with 2 : 2-dimethylpentan-2-one which is formed after isomerisation of the olefin to 2 : 2 : 4-trimethylhex-2-ene. Oxidation of these three olefins by chromic oxide in acetic anhydride was examined to determine if they give epoxides under these conditions. A relatively low yield of epoxide is obtained from 2 : 2 : 4 : 6 : 6-pentamethylhept-3-ene (I*f*). 4-Ethyl-2 : 2-dimethylhex-3-ene (I*e*) gave an even smaller yield; none could be detected in the products of oxidation of 2 : 2 : 4-trimethylhex-3-ene (I*d*).

It is known from previous work [2,6] that the isolation of epoxides from chromic oxide–acetic anhydride oxidations is dependent on a number of factors, resistance to further oxidation and to ring opening being the most important. The above results could therefore be adequately accounted for on the basis of sensitivity of the epoxide were it not for the discrepancy between the relatively high yield of 2-*tert.*-butyl-2 : 4 : 4-trimethylpentanoic acid (III*e*) from 2 : 2 : 4 : 6 : 6-pentamethylhept-3-ene (I*f*) in aqueous chromic acid–sulphuric acid and the poor yield of the aldehyde corresponding to (III*e*) when the epoxide is treated with aqueous sulphuric acid. These observations reinforce the earlier conclusions that the epoxide is not the true intermediate in any of the chromic acid oxidations. Conclusive evidence for this view is provided by observations on some 1 : 1-diaryl-2-methylpropenes; [6] these give epoxides in high yield by reaction with chromic

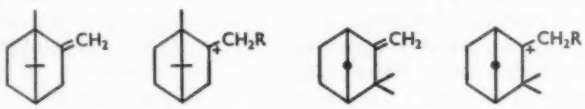
(IV) 



(V)

oxide in acetic anhydride, yet are oxidised by aqueous sulphuric–chromic acid faster than the epoxide is hydrated by aqueous sulphuric acid of the same strength.

It is these observations which have confirmed the view that the epoxide is not the true intermediate in the oxidation, but that in suitable circumstances it can be derived from some addition complex of the olefin and the oxidising agent. In an earlier paper, it was suggested that electrophilic addition of chromic oxide would give a complex of the type (IV), and that all the known ways in which oxidation at the double bond can occur may be adequately represented in terms of such an addition complex.[2] In this formulation (IV) the $O{\cdot}CrO_2$ addendum is representational of any form of oxygenated Cr^{VI} grouping. The possible development of a negative charge on the addendum is ignored.



(VI) (VII) (VIII) (IX)

Zeiss and Zwanzig [7] have suggested an alternative formulation (V) for the initial phase of the reaction between the olefin and chromic acid. They base their choice on the assumption that if (IV) represented the first stage rearrangement should occur in the cyclic system of 1-methyl-α-fenchene (VI); this is not observed when the oxidation is carried out by chromic acid in acetic acid solution. They have argued that because the system (VII; R = H) is prone to rearrangement, the system (VII) when R = OH or $O{\cdot}CrO_2$ should rearrange in the same way. That this argument is not sound can be shown by reference to camphene (VIII). This has been examined in much greater detail than 1-methyl-α-fenchene, and its derived system (IX; R = H) is known to be sensitive to

[6] Hickinbottom and Moussa, *J.*, 1957, 4195.
[7] Zeiss and Zwanzig, *Chem. and Ind.*, 1956, 545.

rearrangement to bornyl derivatives. On the other hand, camphene oxide isomerises to camphenilanaldehyde on treatment with aqueous mineral acid with no recognisable alteration in the ring system.[8] It is reasonably certain that this change occurs through the carbonium ion (IX; R = OH) which is comparable in form with the addition complex (IX; R = O·CrO_2) which we postulated for the initial stage of the oxidation. Further, when camphene is oxidised by chromic oxide in acetic anhydride, camphene oxide is formed; [8] under more drastic conditions, camphenilone and camphenilanic acid are formed without any recognisable alteration in the ring system.[9] Zeiss and Zwanzig's formulation has other disadvantages: it does not explain the oxidative rearrangements which are characteristic of some olefins, such as 2 : 2 : 4 : 6 : 6-pentamethylhept-3-ene, 2 : 2 : 4-trimethylpent-2-ene, or 2 : 4-dimethylpent-2-ene; nor would it have been possible to predict from it the formation of epoxides from olefins by oxidation in anhydrous solvents. A more serious objection lies in its failure to account for the formation of 1 : 4-diketones [10] when some steroidal conjugated dienes are oxidised by dichromate in acetic acid: indeed it prohibits the formation of 1 : 4-diketones. The formal resemblance between the electrophilic addition of halogen or halogen hydrides to conjugated dienes and the results of the oxidation of these dienes by chromic acid is sufficiently striking to make the form of addition of chromic oxide that we have suggested seem more than probable.

Experimental

Oxidation of 2 : 2 : 4 : 6 : 6-*Pentamethylhept-3-ene.*—(a) *By aqueous sulphuric and chromic acid.* The olefin [11] (50 g.) was added in small portions to a stirred mixture of sodium dichromate (180 g.) and aqueous sulphuric acid (60% w/v; 900 c.c.), each portion being allowed to react completely before further addition was made. About 12 hr. were required to complete the addition and the temperature was kept between 30° and 40°. Stirring was continued for 4 hr. after all the olefin had been added; the mixture was then diluted with water (2 l.) and extracted with ether. The acid products, removed from the combined ether extracts by alkali, were separated by distillation into 2 : 2-dimethylpropanoic acid (7·5 g.) (*p*-toluidide, m. p. and mixed m. p. 120°) and 2-*tert.*-butyl-2 : 4 : 4-trimethylpentanoic acid (17·5 g.), m. p. 130° (from acetone) (Found: C, 72·5; H, 12·3%; equiv., 196. Calc. for $C_{12}H_{24}O_2$: C, 72·0; H, 12·1%; equiv., 200). The absence of an appreciable amount of di*neo*pentylacetic acid in the product was demonstrated by treatment successively with thionyl chloride and aqueous ammonia; no amide was formed. Under these conditions di*neo*pentylacetic acid gives an amide; 2-*tert.*-butyl-2 : 4 : 4-trimethylpentanoic acid gives only the free acid (cf. Conant and Wheland [12]). Hence it may be concluded that there is no isomerisation of the olefin during its oxidation.

The butyltrimethylpentanoic acid in concentrated sulphuric acid at 180—200° behaves as a tertiary carboxylic acid, the carboxyl group being eliminated as carbon monoxide (80% yield) during 15 min.

Attempts to reduce the acid by lithium aluminium hydride in boiling ether failed. Reduction of the acid chloride (b. p. 101°/11 mm., n_D^{20} 1·4646; from the acid and boiling thionyl chloride) gave an alcohol which was not characterised except by oxidising it with *tert.*-butyl chromate to 2-*tert.*-butyl-2 : 4 : 4-trimethylpentanal (2 : 4-dinitrophenylhydrazone, needles, m. p. 152—153° not depressed on admixture with a specimen prepared from 3 : 4-epoxy-2 : 2 : 4 : 6 : 6-pentamethylheptane [11]).

The neutral products of the oxidation were resolved by distillation into 4 : 4-dimethylpentan-2-one (b. p. 26—35°/14 mm., n_D^{20} 1·4050—1·4061, 1·5 g.; 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 100—101°) and material of b. p. 80—92°/14 mm., n_D^{20} 1·4310—1·4352 (7·6 g.). The latter material was not homogeneous, but contained a ketone which was characterised by its 2 : 4-dinitrophenylhydrazone {needles, m. p. 134°, after chromatographing on

[8] Hickinbottom and Wood, *J.*, 1953, 1906.
[9] Treibs and Schmidt, *Ber.*, 1928, **61**, 464.
[10] Fieser *et al.*, *J. Amer. Chem. Soc.*, 1951, **73**, 2397; 1953, **75**, 116, 121; Elks, Evans, Long, and Thomas, *J.*, 1954, 452; Budziarek, Newbold, Stevenson, and Spring, *J.*, 1952, 2892; Barton and Laws, *J.*, 1954, 52.
[11] Davis and Hickinbottom, *J.*, 1957, 1998.
[12] Conant and Wheland, *J. Amer. Chem. Soc.*, 1933, **55**, 2502.

alumina [benzene–light petroleum (b. p. 60—80°)] (Found: C, 56·7; H, 6·9; N, 15·4. Calc. for $C_{18}H_{32}O_5N_4$: C, 56·8; H, 7·4; N, 14·7. Calc. for $C_{18}H_{26}O_5N_4$: C, 57·1; H, 6·9; N, 14·8%)}. An oxime, prepared in refluxing pyridine, had m. p. 128—129° (from alcohol). No crystalline semicarbazone could be isolated from the crude carbonyl compound. Miner's carbonyl compound [4] had b. p. 89°/16 mm., n_D^{20} 1·4320, and gave a 2 : 4-dinitrophenylhydrazone, m. p. 133—134°, oxime, m. p. 129—130°, and semicarbazone, m. p. 127—128°.

(b) *By chromic oxide in acetic anhydride.* An ice-cold solution of dried chromic oxide (15 g.) in acetic anhydride (15 c.c.) diluted with carbon disulphide (100 c.c.) was prepared by cautious addition of the chromic oxide–acetic anhydride in 1 c.c. portions to 10 c.c. of carbon disulphide. It is important to keep the reagents at 0° or below during this stage and subsequently, otherwise violent decomposition may occur.

This reagent was added in 1 c.c. portions to the olefin (46 g.) in carbon disulphide (100 c.c.), at −12°, and stirred during the addition and for 3½ hr. afterwards. A heavy dark precipitate was collected, and the filtrate shaken with sodium carbonate solution till neutral, then dried and distilled.

A considerable amount of unchanged olefin, b. p. 60°/12 mm., n_D^{20} 1·4340—1·4385, was obtained. It was followed by a fraction, b. p. 77—84°/12 mm., n_D^{20} 1·4443 (1·6 g.), which was not homogeneous; the presence of epoxide was demonstrated by the formation of the 2 : 4-dinitrophenylhydrazone of 2-*tert.*-butyl-2 : 4 : 4-trimethylpentanal (m. p. and mixed m. p. 152—153°) when it was warmed with aqueous-alcoholic 30% sulphuric acid containing 2 : 4-dinitrophenylhydrazine.

The higher-boiling fractions of the product (4 g.), b. p. 84°/11 mm., n_D^{20} 1·4480, did not give a pure compound.

The forerunnings of the distillation and the contents of the cold trap (1 g.) contained some methyl *neo*pentyl ketone (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 100°).

Oxidation of 2 : 2 : 4-*Trimethylhex*-3-*ene by Aqueous Sulphuric and Chromic Acid.*—The olefin [13] (75 g.) was added to a solution of chromic oxide (270 g.) in aqueous sulphuric acid (60% w/v; 100 c.c.) at 20—30°, as described above for 2 : 2 : 4 : 6 : 6-pentamethylhept-3-ene. The acidic products of the oxidation were 2 : 2-dimethylpropanoic acid (12 g.) and 2-*ethyl*-2 : 3 : 3-*trimethylbutanoic acid* (4·4 g.), b. p. 122—130°/22 mm., m. p. 103—104° (from aqueous alcohol) (Found: C, 68·4; H, 11·4%; equiv., 151. $C_9H_{18}O_2$ requires C, 68·3; H, 11·5%; equiv., 158). This acid gave 75% of the theoretical amount of carbon monoxide when it was heated for ½ hr. with concentrated sulphuric acid at 180—200°.

The neutral products were ethyl methyl ketone (b. p. 70—74°: 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 110—111°) and methyl *neo*pentyl ketone, identified as above. The conditions of the oxidation were varied by adding the oxidising agent [chromic oxide (30 g.) in water (300 c.c.)] to a stirred suspension of the olefin (25 g.) in 70% w/v sulphuric acid (250 c.c.). The acidic products were 2 : 2-dimethylpropanoic acid (1·1 g.) and 2-ethyl-2 : 3 : 3-trimethylbutanoic acid (0·8 g.). From the neutral portion of the product, there were isolated, ethyl methyl ketone (0·5 g.), methyl *neo*pentyl ketone (2·2 g.), and 3 : 5 : 5-trimethylhex-2-one (8 g.), b. p. 80—83°/63 mm., n_D^{20} 1·4190—1·4200 (2 : 4-dinitrophenylhydrazone, m. p. 56—59°, raised to 59—61° on admixture with an authentic specimen).

Oxidation of 4-*Ethyl*-2 : 2-*dimethylhex*-3-*ene.*—(a) *By aqueous sulphuric and chromic acid.* The olefin (70 g.) was added to a stirred solution of sodium dichromate (300 g.) in 60% w/v sulphuric acid (1400 c.c.) at 30—40° during 20 hr. The acid products were resolved by distillation into 2 : 2-dimethylpropanoic acid (20 g., crude) and a semisolid acid, b. p. 130—132°/12 mm. (3·5 g.), which was purified with some loss from aqueous acetone: the pure *acid* melted at 67° (Found: C, 69·7; H, 11·6%; equiv., 167. $C_{10}H_{20}O_2$ requires C, 69·7; H, 11·7%; equiv., 172), and had the characteristics of a tertiary acid; in concentrated sulphuric at 200° 87% of the theoretical amount of carbon monoxide was evolved.

From the neutral products diethyl ketone was isolated (3·8 g.) (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 154°). A second ketone was present in the fraction, b. p. 43—53°/11 mm. (1·4 g.); it was characterised by its 2 : 4-dinitrophenylhydrazone, leaflets [from ethyl acetate–light petroleum (b. p. 60—80°)], m. p. 133—134°, depressed on admixture with 5 : 5-dimethylhexan-3-one 2 : 4-dinitrophenylhydrazone, m. p. 135°.

(b) *By chromic oxide in acetic anhydride.* A solution of chromic oxide (16 g.) in acetic anhydride (16 c.c.) diluted with carbon disulphide (100 c.c.) was added in 1 c.c. portions to

[13] Whitmore *et al.*, *J. Amer. Chem. Soc.*, 1941, **63**, 643.

4-ethyl-2 : 2-dimethylhex-3-ene (56 g.) in carbon disulphide. The products were diethyl ketone (5 g.) (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 154°) and fractions, b. p. 46—68°/17 mm., n_D^{20} 1·4280—1·4290 (9 g.), which could not be efficiently resolved by distillation. By shaking them with aqueous sulphuric acid (0·5%) for 24 hr. and then removing volatile matter, a viscous residue was left having the characteristics of a glycol. It gave, on oxidation by periodic acid, 2 : 2-dimethylpropanal (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 210°) and diethyl ketone (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 154°). A considerable amount of unchanged olefin was recovered, having b. p. 36—46°/17 mm., n_D^{20} 1·4300—1·4291.

The authors thank the Hydrocarbons Research Group of the Institute of Petroleum for support. They also acknowledge assistance given by the Central Research Fund of the University of London in the purchase of special apparatus.

QUEEN MARY COLLEGE, UNIVERSITY OF LONDON,
MILE END ROAD, LONDON, E.1. [*Received, February 4th*, 1958.]

---

450. *Stereochemical Investigations of Cyclic Bases. Part II.* Hofmann Degradation of Some Cyclic Quaternary Ammonium Salts.*

By K. JEWERS and J. MCKENNA.

The factors are reviewed which influence Hofmann degradation of quaternary ammonium salts, particularly in cyclic systems. An examination of the degradation of piperidinium-1-*spiro*-1′-pyrrolidinium hydroxide indicates that the olefin-forming elimination can involve either ring with about equal ease, but that the alternative nucleophilic replacement preferentially opens the pyrrolidine ring. Hofmann elimination of 2 : 2′-dimethylpiperidinium-1-*spiro*-1′-pyrrolidinium hydroxide, *cyclo*hexyldimethyl*cyclo*pentylammonium hydroxide, and (*cyclo*hexylmethyl)dimethyl(*cyclo*pentylmethyl)ammonium hydroxide proceeds mainly in one direction in each case, yielding respectively 2-methyl-1-pent-4′-enylpiperidine, *cyclo*pentene (with *N-cyclo*hexyldimethylamine), and methylene*cyclo*hexane [with dimethyl(*cyclo*pentylmethyl)amine].

HOFMANN degradation of quaternary ammonium hydroxides has been extensively investigated, particularly by Ingold and his collaborators [1] who concluded that in a bimolecular Hofmann elimination the tendency, because of hyperconjugation, for the most highly alkylated olefin to be formed (Saytzeff rule) is effectively opposed by the reduction in acidity of hydrogen atoms caused by increasing alkylation at the carbon atoms carrying them, owing to electron repulsion by the alkyl groups in the electrical field of the quaternary ammonium pole. Degradation of the ammonium hydroxide (I; R, R′, R″, and R‴ = alkyl), for example, would lead to preferential anion-attack at a methyl rather than at a methylene or methine hydrogen atom. This theory would in general predict formation of the " least substituted olefin " (Hofmann rule †) on degradation of quaternary ammonium salts, but a " least substituted olefin " does not always arise from anion-attack on a hydrogen atom attached to the least alkylated carbon β to the quaternary nitrogen atom; furthermore, it would be illogical to interpret, for example, the observed [2] degradation of *cis*- and *trans*-decahydro-1-methylquinoline methohydroxides

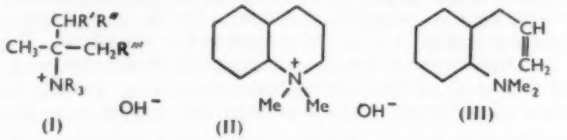
* Part I, *J.*, 1956, 573. A preliminary note on Hofmann fission of heterocyclic bases was published in *Chem. and Ind.*, 1954, 406. Dr. F. E. King's statement made in *J.*, 1954, 3798, footnote, does not accord with my recollection of events or with my interpretation of the facts. J. McK.

† The Hofmann rule in the strictest sense applies to quaternary ammonium salts containing only primary alkyl groups.

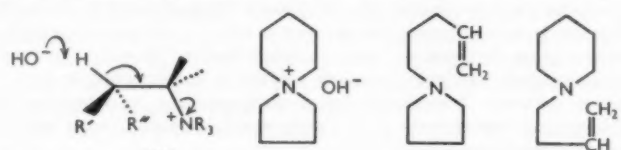
[1] For summary see the chapter on " Olefin-forming Eliminations " in Ingold, " Structure and Mechanism in Organic Chemistry," Bell, London, 1953.

[2] Bailey, Haworth, and McKenna, *J.*, 1954, 967.

(II) to the corresponding 2-allyl*cyclo*hexyldimethylamines (III) by reference to the fact that the unsaturated amines are the " least substituted olefins."



Ingold's interpretation of the departure from Saytzeff eliminatfon observed with quaternary ammonium salts is not accepted by H. C. Brown and his collaborators,[3] who have suggested that steric interaction between the bulky $^+NR_3$ group and groups R', R'' in the intermediate complex (IV; R, R', R'' = alkyl) explains the observed direction of elimination, since the steric interaction is smaller if R' or R'' (or both) is hydrogen. Whatever the relative merits of Ingold's and Brown's interpretation of the results summarised by the Hofmann rule in the acyclic series, a detailed conformational approach is in general required for discussion of the reaction in alicyclic and reduced heterocyclic systems. Relevant well-recognised factors are the normal preference in the transition state for a coplanar *trans*-arrangement of the groups being eliminated and the intervening carbon atoms (as in IV, for example) and the normal greater difficulty of introducing a double bond in a position *endo* or *exo* in relation to a six- rather than a five-membered ring.[4] Double bonds in different positions in the same ring (or in different rings of the same size) in polycyclic systems may also vary considerably in stability.[5] A minor point is that the statistical probabilities of elimination of a methyl, methylene, or methine hydrogen in (I) are altered if the methylene and methine carbon atoms are included in a small ring system, owing to diminished possibilities of free rotation. A further factor of potential

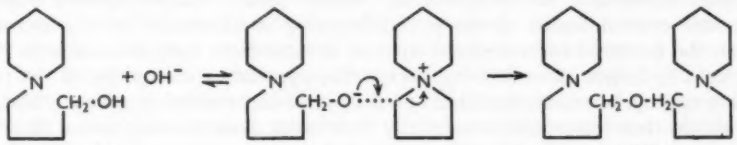


importance in Hofmann degradation of some cyclic quaternary salts is the possibility of formation of a thermodynamically more stable methine, irrespective of opposing kinetic factors which may control the primary reaction, by repeated recyclisation [6] of the primary methine followed by further ring fission or by other secondary changes.[7] This particular aspect is not considered further in the present paper, where the methines derived by pyrolysis of four selected quaternary ammonium hydroxides in all cases appear to be the primary products.

The pyrolysis of piperidinium-1-*spiro*-1'-pyrrolidinium hydroxide (V) was described by von Braun,[8] who obtained a monounsaturated product, $C_9H_{17}N$, b. p. 176—180°, together with a higher-boiling fraction identified as 1-4'-hydroxybutylpiperidine (IX). The unsaturated fraction was thought to be a mixture of 1-pent-4'-enylpyrrolidine (VI) and 1-but-3'-enylpiperidine (VII), and hydrogenation followed by fractional distillation yielded some 1-pentylpyrrolidine. Repetition of this pyrolysis yielded lower- and higher-boiling products analysing respectively as $C_9H_{17}N$ and $C_{18}H_{36}ON_2$. Of these the first

[3] Brown and Moritani, *J. Amer. Chem. Soc.*, 1956, **78**, 2203, and immediately preceding papers by Brown and his collaborators.
[4] Weinstock, Pearson, and Bordwell, *ibid.*, 1956, **78**, 3468; cf. ref. 17.
[5] Cf. Turner, Meador, and Winkler, *ibid.*, 1957, **79**, 4122.
[6] Favre, Haworth, McKenna, Powell, and Whitfield, *J.*, 1953, 1115.
[7] *Inter al.*, Weinstock, *J. Org. Chem.*, 1956, **21**, 540.
[8] von Braun, *Ber.*, 1916, **49**, 2629.

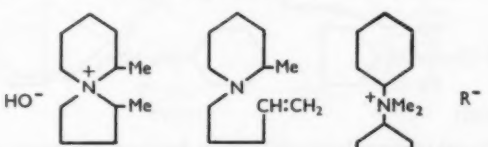
evidently corresponds to von Braun's mixture of unsaturated amines, but the second appeared to be the basic ether (VIII) rather than the alcohol (IX). Such ethers have often been encountered in Hofmann pyrolysis mixtures, and (VIII) could arise from (IX) by further reaction as shown. The constitution of the ether (VIII) was confirmed by fission



(IX) (VIII)

with hydrobromic acid to 1-4′-bromobutylpiperidine hydrobromide. No isomeric hydrobromide was isolated, and this result, together with von Braun's (and, less specifically, with the numerous examples in the literature of similar pyrrolidine ring fission), indicates that the pyrrolidine is more easily opened than the piperidine ring in this type of displacement reaction. In the strongly alkaline medium the reaction is probably synchronous, involving the anion in the rate-determining step, but, irrespective of mechanism, the readier fission of the five-membered ring appears (as in many similar cases) to be related to the ease with which the energetically unfavourable bond oppositions in pyrrolidine can be disturbed; piperidine, like *cyclo*hexane, can be written in a chair conformation with a fully staggered arrangement of carbon–hydrogen bonds.

The unsaturated basic mixture, $C_9H_{17}N$, from the pyrolysis did not appear to undergo cyclisation in hot glacial acetic acid as do [2] other methines, *e.g.*, (III), stereochemically more suitable for such cyclisation. For determination of the ratio of (VI) to (VII), the methine fraction was converted by hydrogenation and methylation into a mixture of 1-pentylpyrrolidine and 1-butylpiperidine methiodides, chromatographic examination of which indicated that the salts were present in equal proportion. The equal ease of fission of the piperidine and the pyrrolidine rings in the olefin-forming decomposition of the *spiro*-quaternary ammonium salt appears to be related to the considerations that the *trans*-coplanar type of intermediate complex (*i.e.*, H–C–C–N^+ coplanar, with H and N^+ *trans*) is possible for the piperidine, but not for the pyrrolidine ring fission, but that, contrariwise, the five-membered pyrrolidine ring with its unfavourable bond oppositions has a greater inherent tendency towards intermediate complex formation if conformational strain is thereby reduced. These two factors are also considered by Weinstock *et al.* in their discussion [4] of the relative ease of *trans*-elimination from *cyclo*pentane and *cyclo*hexane ring systems, with formation of the cyclic olefins; in these eliminations (where the rings are *not* simultaneously broken in the reactions), the two factors do not appear to balance and *cyclo*pentenes are more readily formed.



(X) (XI) (XII)

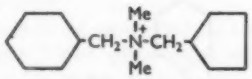
The next base pyrolysed was (X), the 2 : 2′-dimethyl homologue of (V); this structure corresponds to four racemic forms (with varying degrees of internal strain) but the product obtained by condensation of 2-methylpiperidine with 1 : 4-dibromopentane appeared homogeneous; the actual stereochemical structure or homogeneity of our spiran is of little consequence, however, in considerations of its Hofmann fission. When the quaternary hydroxide was pyrolysed no basic alcohol or ether was formed, but an unsaturated base

XUM

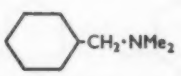
$C_{11}H_{21}N$ was obtained, identified as 2-methyl-1-pent-4'-enylpiperidine (XI) by (*a*) hydrogenation to 2-methyl-1-pentylpiperidine (the methiodide of which, like that of the unsaturated base, was chromatographically homogeneous), (*b*) the infrared spectrum, with bands at 905 and 992 cm.$^{-1}$ (–CH=CH_2),[9] and (*c*) analogy with the pyrolysis of 1 : 2-dimethylpyrrolidinium methohydroxide, which yields dimethylpent-4'-enylamine.[10] The greater ease of fission of the pyrrolidine ring is illustrated by this pyrolysis; in this case the favoured *trans*-coplanar type of intermediate complex can arise by anion-attack on a hydrogen atom forming part of the pyrrolidine methyl (or of the piperidine methyl or appropriate methylene) but not of a pyrrolidine methylene group. The observed fission should therefore occur more readily than *either* olefin-forming fission observed with the quaternary hydroxide (V). The lack of formation of a basic alcohol or ether on pyrolysis of the hydroxide (X) is in agreement with this reasoning, since hydroxyl attack on the β-methylene carbon atom in the pyrrolidine ring of (X) should take place with about the same ease as the reaction leading ultimately to the basic ether (VIII).

Preliminary attempts to synthesise *cyclo*hexyldimethyl*cyclo*pentylammonium bromide (XII; R = Br) by reaction of *cyclo*pentyl bromide with *cyclo*hexyldimethylamine resulted only in elimination of hydrogen bromide from the *cyclo*pentyl bromide, which has been shown, however, to undergo condensation as well as elimination with aniline and piperidine.[11] *cyclo*Hexyl bromide reacted in a similar manner. *cyclo*Hexylmethyl*cyclo*pentylamine was synthesised by a method analogous to that used for related amines by Norton and his collaborators:[12] the ketimine derived from *cyclo*pentylamine and *cyclo*hexanone was reduced with hydrogen in presence of Raney nickel, and the resultant secondary base methylated with formaldehyde and formic acid. Pyrolysis of the related quaternary ammonium hydroxide (XII; R = OH) yielded almost exclusively *cyclo*pentene and *cyclo*hexyldimethylamine (the base from the reaction mixture was shown by vapour-phase chromatography to contain about 5% of dimethyl*cyclo*pentylamine). The bulky quaternary ammonium group is clearly attached to the *cyclo*hexane ring by an equatorial link, so that the geometry of the molecule does not favour formation of *cyclo*hexene by *trans*-elimination.[13]

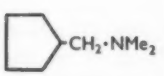
We also examined the pyrolysis of (*cyclo*hexylmethyl)dimethyl(*cyclo*pentylmethyl)-ammonium hydroxide (XIII; R = OH). Methyl*cyclo*pentylamine was prepared by a modification of a previous method;[14] in addition, generous supplies of the amine and its *N*-benzoyl derivative were kindly given to us by Imperial Chemical Industries Limited, Dyestuffs Division, Blackley, Manchester, whom we thank also for helpful advice on the preparation and characterisation of the amine. Condensation of the base with *cyclo*hexanecarbonyl chloride, and reduction of the resulting amide with lithium aluminium hydride gave (*cyclo*hexylmethyl)(*cyclo*pentylmethyl)amine, from which the ammonium salt (XIII; R = I) was prepared by methylation with formaldehyde and formic acid followed by reaction of the product with methyl iodide.



(XIII)



(XIV)



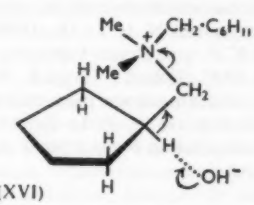
(XV)

Pyrolysis of the quaternary hydroxide gave basic and neutral products. Fractional distillation of the former yielded (*cyclo*hexylmethyl)methyl(*cyclo*pentylmethyl)amine and a smaller lower-boiling fraction from which pure samples of only dimethyl(*cyclo*-pentylmethyl)amine picrate or methiodide were obtained on fractional crystallisation of

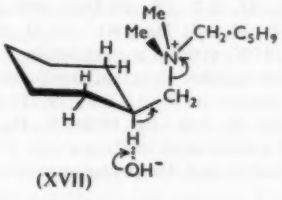
[9] Bellamy, "The Infra-Red Spectra of Complex Molecules," Methuen, London, 1954, p. 31.
[10] Ladenburg, Mugdan, and Brzostovicz, *Annalen*, 1893, **279**, 344.
[11] Loevenich, Utsch, Moldrickx, and Schaefer, *Ber.*, 1929, **62**, 3084.
[12] Norton, Haury, Davis, Mitchell, and Ballard, *J. Org. Chem.*, 1954, **19**, 1054.
[13] Cf. Haworth, McKenna, and Powell, *J.*, 1953, 1110; Gent and McKenna, *J.*, 1956, 573.
[14] von Braun and Anton, *Ber.*, 1933, **66**, 1374.

the crude salts. Vapour-phase chromatography of the unfractionated basic product from the Hofmann decomposition showed, however (by comparison of the results with those obtained with synthetic mixtures), that (*cyclo*hexylmethyl)dimethylamine (XIV) was present along with the dimethyl(*cyclo*pentylmethyl)amine (XV) in the molar ratio of *ca.* 1 : 2. After ozonolysis of the hydrocarbon fraction from the degradation, only *cyclo*hexanone was identified (as 2 : 4-dinitrophenylhydrazone); this is clearly derived from methylene*cyclo*hexane, but vapour-phase chromatography showed the presence in the hydrocarbon fraction of a smaller proportion of a more easily eluted (probably more volatile) component, in agreement with the complementary results of the analysis of the basic fraction. We did not have samples of methylene*cyclo*pentane and methylene*cyclo*hexane for comparative chromatograms, but the more volatile component is obviously mainly the former hydrocarbon, although the recent work of Cope and his collaborators [15] on Hofmann degradation of the methohydroxides of (XIV), (XV), and related compounds suggests that the hydrocarbon mixture may have contained also a little 1-methyl*cyclo*pentene. It is clear, however, that the most important mode of olefin-forming decomposition of the quaternary hydroxide (XIII; R = OH) is fission between the quaternary nitrogen atom and the *cyclo*hexylmethyl group, and this result accords with the American authors' work which shows that degradation of the methohydroxide of (XIV) to methylene*cyclo*hexane is smoother than the analogous decomposition of the methohydroxide of (XV).

It is of interest to consider the observed pyrolysis of (*cyclo*hexylmethyl)dimethyl(*cyclo*pentylmethyl)ammonium hydroxide from the standpoint of a generalisation proposed in 1954 by H. C. Brown and his collaborators [16] regarding the relative ease of introduction of a double bond into a position *exo* to a six- or a five-membered reduced ring; after some criticism and misunderstanding the following revised statement was recently [17] given by Brown. "Double bonds which are *exo* to a 5-ring are less reactive and more stable (relative to the saturated derivatives) than related double bonds which are *exo* to a 6-ring. Reactions which involve the formation or retention of an *exo* double bond in a 5-ring derivative will be favoured over corresponding reactions which involve the formation or retention of an *exo* double bond in a 6-ring derivative. Reactions which involve the loss of an *exo* double bond will be favoured in the 6-ring as compared to the corresponding 5-ring derivative." This generalisation correlates a wide range of observations, and is in accord with the recently determined [18] heats of hydrogenation of methylene*cyclo*pentane and methylene*cyclo*hexane. Since methylene*cyclo*hexane, however, is preferentially formed on pyrolysis of (*cyclo*hexylmethyl)dimethyl(*cyclo*pentylmethyl)ammonium hydroxide, the second sentence in Brown's statement must be regarded only as one factor



(XVI)



(XVII)

which can affect the course of a reaction but which may be offset by others. The observed preferential course of the pyrolysis is probably due to the hindrance arising between the quaternary ammonium group and the *cis*-hydrogen atoms attached to adjacent *cyclo*pentane carbon atoms in the intermediate complex (XVI) if the usual *trans*-coplanarity requirement of H–C–C–N$^+$ is met; the hindrance is less in the intermediate complex

[15] Cope, Bumgardner, and Schweizer, *J. Amer. Chem. Soc.*, 1957, **79**, 4729.
[16] Brown, Brewster, and Shechter, *ibid.*, 1954, **76**, 467.
[17] Brown, *J. Org. Chem.*, 1957, **22**, 439.
[18] Turner and Garner, *J. Amer. Chem. Soc.*, 1957, **79**, 253.

(XVII) leading to methylene*cyclo*hexane formation, since the bulky group which includes the quaternary nitrogen is expected to be equatorial. The transition states are here pictured with geometries resembling those of the reactants [3] (as also in formula IV), but the moderate proportion of fission products formed in accordance with Brown's rule [*i.e.*, methylene*cyclo*pentane and (*cyclo*hexylmethyl)dimethylamine] affords an indication of the degrees to which the double bonds have developed.[19] The formation of 2-methyl-1-pent-4′-enylpiperidine (XI) rather than 1-hex-5′-enyl-2-methylpyrrolidine on pyrolysis of the ammonium hydroxide (X) may be regarded as an example of the Brown rule, the incipient double bond being formed *exo* to the partly opened 5-ring rather than the partly opened 6-ring.

Degradation of some fused polycyclic quaternary ammonium hydroxides will be considered in later publications.

Experimental

Degradation of Piperidinium-1-spiro-1′-*pyrrolidinium Hydroxide.*—The appropriate quaternary bromide [20] (7·9 g.) was converted into the hydroxide by the silver oxide method, and this was heated at 140° (bath) for 0·5 hr. during which decomposition occurred and some volatile base distilled. Distillation was completed by raising the temperature. The distillate and still-residue, on extraction with ether, yielded a product (3·8 g.) from which by fractional distillation were obtained a fraction (1·8 g.), b. p. 170—180° (bath), unsaturated to acid permanganate (Found: C, 77·3; H, 11·7; N, 9·7. Calc. for $C_9H_{17}N$: C, 77·7; H, 12·2; N, 10·1%), and *di*-(4-*piperidinobutyl*) *ether* (VIII) (0·9 g.), b. p. 80—100° (bath)/0·6 mm. (Found: N, 9·7. $C_{18}H_{36}ON_2$ requires N, 9·5%), characterised as the *picrate*, yellow needles (from ethanol), m. p. 188° (Found: C, 48·1; H, 5·9; N, 14·9. $C_{30}H_{42}O_{15}N_8$ requires C, 47·7; H, 5·6; N, 14·9%). The still-residue contained some undecomposed quaternary hydroxide, isolated as picrate [21] (230 mg.), m. p. 232°.

Examination of the Basic Fraction, $C_9H_{17}N$.—When the base (128 mg.) was refluxed in acetic acid (10 c.c.) for 2·5 hr. no quaternary salt was isolated but the original base (116 mg.) was recovered. Attempted fractional crystallisation of the mixed picrates, m. p. 102—107° (Found: C, 49·0; H, 5·3; N, 15·0. Calc. for $C_{15}H_{20}O_7N_4$: C, 48·9; H, 5·5; N, 15·2%), was unsuccessful. Hydrogenation of the base (527 mg.) in ethanol (10 c.c.) in presence of 10% palladium–charcoal (460 mg.) was complete in 1 hr.; the mixture of saturated bases, b. p. 170—180° (bath) (Found: C, 76·6; H, 13·8; N, 9·7. Calc. for $C_9H_{19}N$: C, 76·6; H, 13·5; N, 9·9%), yielded a mixture of methiodides, m. p. 164—166°.

Analysis of the Methiodide Mixture, m. p. 164—166°.—From 1-*n*-butylpiperidine,[22,23] b. p. 176°, were obtained samples of methiodide, m. p. 198° (von Braun [23] gives m. p. 199°), *picrolonate*, yellow needles (from ethanol), m. p. 161° (Found: C, 56·2; H, 6·9; N, 17·1. $C_{19}H_{27}O_5N_5$ requires C, 56·3; H, 6·7; N, 17·3%), and p-*azobenzenebenzylobromide*, orange solid, m. p. 188—190° (Found: N, 9·8; Br, 19·4. $C_{22}H_{30}N_3Br$ requires N, 10·1; Br, 19·2%). 1-*n*-Pentylpyrrolidine, b. p. 176°, yielded a methiodide, m. p. 173° (von Braun [8] gives m. p. 169—170°), a *picrolonate*, yellow needles (from ethanol), m. p. 140° (Found: C, 56·2; H, 6·7; N, 17·1. $C_{19}H_{27}O_5N_5$ requires C, 56·3; H, 6·7; N, 17·3%), and an orange p-*azobenzenebenzylobromide*, m. p. 140° (Found: N, 9·9; Br, 19·3. $C_{22}H_{30}N_3Br$ requires N, 10·1; Br, 19·2%).

The observed variation of melting range with composition for mixtures of the methiodides of 1-*n*-butylpiperidine and 1-*n*-pentylpyrrolidine was:

1-*n*-Pentylpyrrolidine methiodide (%)	90	75	60	50	40	30
Melting range	166—173°	166—171°	166—170°	164—166°	165—175°	165—180°

Methanol solutions (6 mg./c.c.) were prepared of the methiodide mixture, m. p. 164—166°, from the degradation, and of "synthetic" mixtures of 1-*n*-butylpiperidine and 1-*n*-pentylpyrrolidine methiodides in ratios 1 : 1, 1 : 2, and 2 : 1. Spots of these solutions were placed

[19] Cf. Cram, Greene, and Depuy, *J. Amer. Chem. Soc.*, 1956, **78**, 790.
[20] von Braun, *Ber.*, 1916, **49**, 966.
[21] Albert, *Ber.*, 1909, **42**, 545.
[22] von Braun, *Ber.*, 1907, **40**, 3914.
[23] *Idem*, *Ber.*, 1909, **42**, 2532.

on sheets of Whatman's No. 1 filter paper, and the chromatogram developed (upward flow) for 24 hr. with butan-1-ol saturated with water. After being dried, the paper was sprayed with a silver nitrate–dichlorofluorescein solution to mark the position of the methiodide spots. 1-*n*-Butylpiperidine methiodide had R_F 0·51 and 1-*n*-pentylpyrrolidine methiodide had R_F 0·60. The reduced methiodide mixture from the degradation gave a chromatogram similar to that obtained from the 1 : 1 " synthetic " mixture and different from either of the other two. Only partial separation of the *p*-azobenzenebenzylobromides of the saturated amines could be achieved by paper chromatography using *cyclo*hexane–propan-2-ol–acetic acid for development.

Fission of the Base $C_{18}H_{36}ON_2$.—The base (154 mg.) was refluxed with concentrated hydrobromic acid (10 c.c.) for 2 hr., the acid was removed *in vacuo*, and the residue was washed with ether and crystallised from acetone–ether, yielding leaflets of 1-4′-bromobutylpiperidine hydrobromide [21] (207 mg.), m. p. 162° (Found: C, 35·4; H, 6·1; N, 4·6. Calc. for $C_9H_{19}NBr_2$: C, 35·9; H, 6·4; N, 4·7%).

Hofmann Degradation of 2 : 2′-*Dimethylpiperidinium*-1-spiro-1′-*pyrrolidinium Hydroxide*.—1 : 4-Dibromopentane (6·9 g.), 2-methylpiperidine (3 g.), sodium hydroxide (1·2 g.), and water (45 c.c.) were heated together on a steam-bath for 2 hr. with frequent shaking. The mixture was cooled, and the quaternary bromide was precipitated by addition of 10N-sodium hydroxide (60 c.c.) and extracted with chloroform, from which it was precipitated by ether as a hygroscopic solid, m. p. 74°. Addition of ethanolic picric acid to an aqueous solution of the quaternary hydroxide, prepared in the usual way (Ag_2O), gave 2 : 2′-*dimethylpiperidinium*-1-spiro-1′-*pyrrolidinium picrate*, yellow needles (from ethanol), m. p. 249—251° (Found: C, 51·9; H, 6·3; N, 14·3. $C_{17}H_{24}O_7N_4$ requires C, 51·5; H, 6·1; N, 14·1%). An aqueous solution of quaternary hydroxide derived from quaternary bromide (6·9 g.) was evaporated, the residue was decomposed in a bath maintained at 140°, and the volatile products were distilled. Extraction of the distillate and still-residue with ether gave 2-*methyl*-1-*pent*-4′-*enylpiperidine* (3·65 g.), b. p. 200° (bath) (Found: N, 8·2. $C_{11}H_{21}N$ requires N, 8·4%), characterised as the *picrate*, yellow needles (from ethanol), m. p. 72—73° (Found: C, 51·6; H, 6·2; N, 14·4. $C_{17}H_{24}O_7N_4$ requires C, 51·5; H, 6·1; N, 14·1%). Extraction of the still-residue with ethanol gave a little of the original quaternary hydroxide characterised as the picrate, m. p. 249—251°. No quaternary salt was isolated when the unsaturated base (110 mg.) was refluxed in glacial acetic acid (5 c.c.) for 4 hr.; the recovered base (107 mg.) was identified by conversion into the picrate. Hydrogenation of the unsaturated base (525 mg.) in ethanol (10 c.c.) in presence of 10% palladium–charcoal (278 mg.) was complete in 1 hr.; the resulting 2-*methyl*-1-*pentylpiperidine* had b. p. 200° (bath) (Found: C, 78·2; H, 13·9; N, 8·2. $C_{11}H_{23}N$ requires C, 78·0; H, 13·6; N, 8·3%) and yielded a *methiodide*, prismatic needles (from acetone), m. p. 196—198° (Found: C, 46·2; H, 8·2; N, 4·5. $C_{12}H_{26}NI$ requires C, 46·3; H, 8·4; N, 4·5%) undepressed with a specimen prepared as described below.

2-*Methyl*-1-*pentylpiperidine*.—2-Methylpiperidine (5 g.), *n*-pentyl bromide (9 g.), and potassium hydroxide (5 g.) were heated together in a sealed tube at 125° for 24 hr. After being cooled, the mixture was acidified, and excess of pentyl bromide was extracted with ether. The base, recovered from the acid solution, had b. p. 206° (Found: C, 78·5; H, 13·7; N, 8·2. Calc. for $C_{11}H_{23}N$: C, 78·0; H, 13·6; N, 8·3%); the methiodide (Found: C, 46·2; H, 8·3; N, 4·5. Calc. for $C_{12}H_{26}NI$: C, 46·3; H, 8·4; N, 4·5%) had m. p. 196—198°. The tertiary base, b. p. 92—93°/16 mm., has been prepared previously by a different method.[24]

1-n-*Hexyl*-2-*methylpyrrolidine*.—A mixture of 1 : 4-dibromopentane (6 g.), *n*-hexylamine (7·8 g.), and ethanol (50 c.c.) was refluxed for 5 hr., acidified with hydrochloric acid, and evaporated to dryness. The residue was treated with benzoyl chloride and excess of sodium hydroxide solution to remove primary or secondary amines; the residual 1-n-*hexyl*-2-*methylpyrrolidine* had b. p. 202—204° (Found: C, 77·6; H, 13·8; N, 8·0. $C_{11}H_{23}N$ requires C, 78·0; H, 13·6; N, 8·3%) and yielded a *methiodide*, plates (from acetone–ether), m. p. 130—131° (Found: C, 46·7; H, 8·4; N, 4·6; I, 40·3. $C_{12}H_{26}NI$ requires C, 46·3; H, 8·4; N, 4·5; I, 40·8%).

Preparation of cyclo*Hexyldimethyl*cyclo*pentylammonium Iodide*.—*cyclo*Pentanone (50 g.) and *cyclo*hexylamine (59 g.) were refluxed in dry benzene (100 c.c.) in an apparatus with a phase-separation head until, after 24 hr., water (11 c.c.) had separated. The resulting ketimine (65·6 g.), b. p. 110—115°/15 mm., was freed from unchanged more volatile reactants and hydrogenated at 150°/50 atm. in presence of Raney nickel (5 g.). The product was fractionally distilled to separate traces of hydrogenolysis products, and the cyclo*hexyl*cyclo*pentylamine*

[24] Paden and Adkins, *J. Amer. Chem. Soc.*, 1936, **58**, 2487.

(52 g.), b. p. 118—120°/17 mm. (Found: N, 8·1. $C_{11}H_{21}N$ requires N, 8·4%), was methylated on the steam-bath for 4 hr. with 90% formic acid (87 g.) and 40% aqueous formaldehyde (30 g.). The resulting tertiary base (47 g.) was converted with methyl iodide into cyclo*hexyldimethyl*-cyclo*pentylammonium iodide*, which was obtained as needles, m. p. 221—222°, from acetone (Found: C, 47·7; H, 8·1; N, 4·4; I, 39·4. $C_{13}H_{26}NI$ requires C, 48·3; H, 8·1; N, 4·3; I, 39·3%).

Hofmann Degradation of cyclo*Hexyldimethyl*cyclo*pentylammonium Hydroxide.*—The aqueous quaternary hydroxide solution from the above iodide (6 g.) was concentrated to small volume and kept at 140° in a distillation apparatus fitted with a cold trap (solid carbon dioxide) for 0·5 hr., during which decomposition took place. The temperature was then slowly increased until all volatile products had distilled, and the distillate was separated into a neutral (0·75 g.) and a basic (2·02 g.) fraction. The latter had b. p. 164—165° and yielded a picrate, m. p. 176°, and a methiodide, m. p. 260—262°, identified (mixed m. p.) as salts of *cyclo*hexyldimethylamine. Vapour-phase chromatography of the basic fraction on a Celite–silicone column at 107° with a nitrogen flow of 52 c.c. per min. showed (by comparison of the potentiometer record from the katharometer with those derived from control mixtures of the components) that the fraction consisted of *cyclo*hexyldimethylamine (95%; retention time 27·5 min.) and dimethyl-*cyclo*pentylamine (5%; retention time 10·0 min.).

The very volatile neutral fraction, after being dried with sodium, had n_D^{25} 1·4230 (lit.:[25] *cyclo*hexene n_D^{25} 1·4438; *cyclo*pentene n_D^{25} 1·4194). Circumstances prevented examination by vapour-phase chromatography, but oxidation of the neutral fraction (0·35 g.) in acetone (50 c.c.) at 20° with finely powdered potassium permanganate (3·5 g.) which was gradually added, with continuous stirring, during 4 hr. gave glutaric acid (384 mg.), m. p. (from benzene) and mixed m. p. 95° (Found: C, 45·4; H, 6·3. Calc. for $C_5H_8O_4$: C, 45·5; H, 6·1%).

(cyclo*Pentylmethyl*)*amine.*—*cyclo*Pentylacetic acid (14·5 g.) was converted with thionyl chloride into the acid chloride (14·8 g.), b. p. 176—178°, which was added to a suspension of sodium azide (7 g.) in dry benzene (150 c.c.), the mixture was refluxed for 20 hr., cooled, and filtered, and the filtrate was refluxed with concentrated hydrochloric acid (60 c.c.) for 2·5 hr. The base (5·5 g.) obtained from the resulting hydrochloride had b. p. 140°, and with ethyl oxalate gave the *oxamide*, needles [from benzene–petroleum (b. p. 60—80°)], m. p. 191° (Found: C, 66·5; H, 9·8; N, 11·5. $C_{14}H_{24}O_2N_2$ requires C, 66·6; H, 9·6; N, 11·1%).

Dimethyl(cyclo*pentylmethyl*)*amine.*—The above primary amine (1·5 g.) was heated on a water-bath for 4 hr. with 90% formic acid (4 g.) and 40% formaldehyde (2·5 g.). The resulting dimethyl(*cyclo*pentylmethyl)amine, b. p. 146°, was characterised as the picrate, m. p. 142° (Found: C, 47·0; H, 5·8; N, 16·0. Calc. for $C_{14}H_{20}O_7N_4$: C, 47·2; H, 5·7; N, 15·7%), and the methiodide, m. p. 200—202° (Found: C, 40·0; H, 7·3; N, 5·3. Calc. for $C_9H_{20}NI$: C, 40·2; H, 7·2; N, 5·2%). Methylation of the primary amine with formaldehyde and dilute formic acid gave a tertiary base with the same properties. Treatment of the tertiary base with benzoyl chloride and alkali did not affect the properties of its derivatives. The methiodide, m. p. 200—202°, was obtained directly from (*cyclo*pentylmethyl)amine by refluxing it (407 mg.) in acetone (50 c.c.) with methyl iodide (3 c.c.) and potassium carbonate (5·6 g.) for 12 hr. This methiodide (0·5 g.) in dry tetrahydrofuran [26] (50 c.c.) was refluxed with lithium aluminium hydride (0·5 g.) for 72 hr. with stirring. The resulting tertiary base (96 mg.) yielded a picrate and a methiodide identical with those described above. This detailed characterisation of dimethyl-(*cyclo*pentylmethyl)amine and its derivatives was effected partly because Mousseron and his collaborators have recorded [27] m. p. 168—169° for the picrate of the tertiary base (prepared from *cyclo*pentanealdehyde). After our work had been completed, however, Cope and his collaborators described the preparation of the amine by a different method [15] and gave m. p. 142·8—143·8° for the picrate.

(cyclo*Hexylmethyl*)*methyl*(cyclo*pentylmethyl*)*amine.*—*cyclo*Pentylmethyl)amine (4 g.), *cyclo*-hexanecarbonyl chloride (7 g.), and excess of 2N-sodium hydroxide were shaken together for 20 min., and the N-cyclo*hexanecarbonyl*(cyclo*pentylmethyl*)*amine* (8·5 g.) recrystallised from light petroleum (b. p. 40—60°) as needles, m. p. 108—110° (Found: C, 74·3; H, 10·9; N, 6·5. $C_{13}H_{23}ON$ requires C, 74·6; H, 11·1; N, 6·7%). The amide (9·5 g.) was reduced (Soxhlet method) with lithium aluminium hydride (2·8 g.) in ether (500 c.c.) during 10 hr., and the

[25] Rossini, Mair, and Streiff, "Hydrocarbons from Petroleum," Reinhold, New York, 1953, p. 234.
[26] Cf. Cope and Bumgardner, *J. Amer. Chem. Soc.*, 1957, **79**, 960.
[27] Mousseron, Jacquier, and Zagdoun, *Bull. Soc. chim. France*, 1952, 197.

(*cyclo*hexylmethyl)(*cyclo*pentylmethyl)amine (4·2 g.), b. p. 264—266°, was characterised as the *hydrochloride*, plates (from acetone), m. p. 234—236° (Found: N, 5·8; Cl, 15·0. $C_{13}H_{26}NCl$ requires N, 6·0; Cl, 15·3%), and the *hydrobromide*, plates (from acetone), m. p. 280° (Found: C, 56·5; H, 9·5; N, 4·8. $C_{13}H_{26}NBr$ requires C, 56·5; H, 9·5; N, 5·1%). The secondary base (9·8 g.) on methylation with 40% formaldehyde (9 g.) and 85% formic acid (13·8 g.) for 3 hr. at 100° gave (*cyclo*hexylmethyl)methyl(*cyclo*pentylmethyl)amine (8 g.), b. p. 265—270°, characterised as the *picrate*, yellow needles (from ethanol), m. p. 110—112° (Found: C, 54·6; H, 7·0; N, 12·9. $C_{20}H_{30}O_7N_4$ requires C, 54·8; H, 6·9; N, 12·8%), and the *methiodide*, prismatic needles (from acetone), m. p. 167—168° (Found: C, 51·0; H, 8·5. $C_{15}H_{30}NI$ requires C, 51·3; H, 8·6%).

Hofmann Degradation of (cyclo*Hexylmethyl*)*dimethyl*(cyclo*pentylmethyl*)*ammonium Hydroxide*.—An aqueous solution of methohydroxide derived from methiodide (5·4 g.) was concentrated and decomposed at 140°, and the products were distilled into a receiver fitted with a cold trap. The distillate was separated into a neutral (394 mg.) and a basic (2·17 g.) fraction. The neutral fraction had n_D^{22} 1·4440 (lit.: methylene*cyclo*pentane [28] n_D^{20} 1·4354; methylene*cyclo*hexane [29] n_D^{20} 1·4502). Vapour-phase chromatography of the neutral fraction on a Celite–silicone column at 87°, with a nitrogen flow of 45 c.c. per min., showed two peaks corresponding to retention times of 5 min. 56 sec. and 12 min. 34 sec. respectively; the area of the second peak was approximately twice that of the first. Ozonolysis of the neutral fraction in *n*-hexane at −70°, and decomposition of the ozonide by boiling water, gave a ketone which yielded a dinitrophenylhydrazone, m. p. 136—146°. From this on fractional crystallisation was obtained only *cyclo*hexanone 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 156—157°.

The basic product (2 g.) from the Hofmann degradation was separated into fractions, b. p. 160° (bath) (0·6 g.) and b. p. 260° (0·75 g.). The first fraction yielded a crude picrate, m. p. 130—137°, and a crude methiodide, m. p. 180—190°, from which were obtained by fractional crystallisation the picrate, m. p. 141—142° (Found: C, 47·5; H, 6·1; N, 15·6. Calc. for $C_{14}H_{20}O_7N_4$: C, 47·2; H, 5·7; N, 15·7%), and the methiodide, m. p. 200°, of dimethyl(*cyclo*pentylmethyl)amine, identified by m. p. and mixed m. p. The second fraction yielded (*cyclo*hexylmethyl)dimethyl(*cyclo*pentylmethyl)amine picrate, m. p. and mixed m. p. 110°.

A vapour-phase chromatogram of a sample (13·0 mg.) of the total base fraction from the Hofmann degradation, in benzene (0·2 c.c.), run on a Celite–silicone column at 131° (with a nitrogen flow of 37 c.c. per min.) showed two bands with retention times 13 min. 45 sec. and 20 min. 38 sec.; these were shown to correspond to dimethyl(*cyclo*pentylmethyl)amine and (*cyclo*hexylmethyl)dimethylamine [30] respectively by experiments with mixtures of these bases, and band-area comparisons indicated that the 13 mg. specimen contained 3·9 mg. of dimethyl(*cyclo*pentylmethyl)amine and 2·0 mg. of (*cyclo*hexylmethyl)dimethylamine. At the column temperature chosen (for satisfactory analysis of the more volatile amines) the third component of the Hofmann mixture was eluted too slowly for analysis, but, by difference, its weight in the sample was 7·1 mg.

We thank the Department of Scientific and Industrial Research for a maintenance grant (to K. J.), Imperial Chemical Industries Limited for the assistance indicated, and Dr. J. M. Tedder for advice on vapour-phase chromatography.

THE UNIVERSITY, SHEFFIELD, 10. [*Received, November 29th*, 1957.]

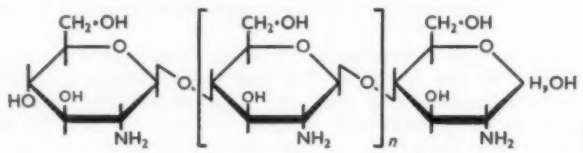
[28] Arnold, Amidon, and Dodson, *J. Amer. Chem. Soc.*, 1950, **72**, 2871.
[29] Egloff in "Physical Constants of Hydrocarbons," Vol. II, Reinhold, New York, 1940, p. 160.
[30] Jaquier, Mousseron, Mousseron-Canet, and Zagdoun, *Bull. Soc. chim. France*, 1952, 1042.

451. *Amino-sugars and Related Compounds. Part IV.* Isolation and Properties of Oligosaccharides obtained by Controlled Fragmentation of Chitin.†*

By S. A. Barker, A. B. Foster, M. Stacey, and J. M. Webber.

Graded acidic hydrolysis of chitosan (obtained by alkaline deacetylation of chitin) followed by selective *N*-acetylation of the fragments yields a mixture of saccharides of which the first seven members have been isolated by chromatography. Evidence is presented which suggests that the saccharides constitute a polymer-homologous series. Structural information on the di- and tri-saccharides is provided by periodate oxidation.

Nomenclature.—Chitin is a substituted polysaccharide since it contains acetylated amino-groups and the logical nomenclature for saccharides derived from chitin should be based on the unsubstituted (*i.e.*, de-*N*-acetylated) polysaccharide. De-*N*-acetylated chitin is widely referred to in the literature as chitosan and it is therefore suggested that the saccharides represented by the general formula (A) be termed chitosaccharides, *e.g.*, chitobiose ($n = 0$), chitotetraose ($n = 2$), etc.



(A)

The saccharides containing one acetyl group on each nitrogen atom, which are the true fragments of chitin, may then be described as tri-*N*-acetylchitotriose, penta-*N*-acetylchitopentaose, etc.

The description of non-uniformly substituted saccharides would require that the constituent monosaccharide units of the oligosaccharides be numbered from the reducing moiety (or modification thereof) so that substituents could be described (*a*) in the accepted manner to indicate their nature and point of attachment to a monosaccharide unit, and (*b*) by a superscript numeral to indicate the position, in the oligosaccharide chain, of the monosaccharide unit to which the substituent is attached. Thus partial *N*-acetylation of chitotriose might yield di-$N^{1,3}$-acetylchitotriose. This system is capable of general extension to chitosaccharide derivatives.

A possibility of confusion would be eliminated if the use of the trivial name chitose for 2 : 5-anhydro-D-mannose were discontinued.

Degradation of chitin by various methods has yielded the following characterised fragments: 2-acetamido-2-deoxy-D-glucose,[1] 2-amino-2-deoxy-D-glucose hydrochloride,[2] di-*N*-acetylchitobiose,[3] chitobiose octa-acetate,[4] and chitotriose hendeca-acetate.[4] Recently Horowitz *et al.*[5] reported that the graded acidic hydrolysis of chitosan (de-*N*-acetylated chitin) yields a series of saccharides which may be fractionated by elution from ion-exchange resins. Only the disaccharide (chitobiose) of this series was isolated and

* Part III, *J.*, 1958, 1890.

† A preliminary report of some of these results has been given in *Chem. and Ind.*, 1957, 208.

[1] Fränkel and Kelly, *Monatsh.*, 1902, **23**, 123.

[2] Ledderhose, *Ber.*, 1876, **9**, 1200.

[3] Zilliken, Braun, Rose, and György, *J. Amer. Chem. Soc.*, 1955, **77**, 1296.

[4] Zechmeister and Tóth, *Ber.*, 1931, **64**, 2028; 1932, **65**, 161.

[5] Horowitz, Blumenthal, Seppala, and Roseman, *Fed. Proc.*, 1955, **14**, 229; Horowitz, Blumenthal, and Roseman, *J. Amer. Chem. Soc.*, 1957, **79**, 5046.

XUM

characterised (as octa-acetate). We now report a partial degradation of chitin which permits the isolation of a series of *N*-acetylated chitosaccharides up to at least the hepta-saccharide.

The chitin used was isolated from the shell of the edible crab, *Cancer pagurus*. Insolubility complicates the controlled fragmentation. Preliminary attempts, by dissolution in strong mineral acid (*e.g.*, concentrated hydrochloric acid saturated at 0° with hydrogen chloride, concentrated sulphuric acid), were unsatisfactory because of the large excess of acid required; concentrated sulphuric acid caused extensive sulphation.

Our acetolysis [6] of chitin gave only chitobiose octa-acetate (in low yield), although it was later shown that tri-*N*-acetylchitotriose with pyridine and acetic anhydride yielded a crystalline product.

Catalytic de-*O*-acetylation (Zemplén) of chitobiose octa-acetate and 2-acetamido-1 : 3 : 4 : 6-tetra-*O*-acetyl-2-deoxy-α- and -β-D-glucose afforded in each case a mixture of at least five components, revealed by paper chromatography. The result was similar when 2-acetamido-2-deoxy-D-glucose was treated under the de-*O*-acetylation conditions. The artefacts in each case had R_F values greater than that of the saccharide from which they were formed. Comparable results have been reported by Zilliken *et al.*[3]

Multiple fractionation, on charcoal–Celite,[7] of the complex mixture obtained by de-*O*-acetylation of a mixture of acetylated lower chitosaccharides, isolated after acetolysis of chitin, gave crystalline di-*N*-acetylchitobiose and tri-*N*-acetylchitotriose. However, the low overall yields and tedious isolation largely deprive the acetolysis method of preparative value.

In a parallel fractionation of the products obtained on catalytic de-*O*-acetylation of a mixture of acetylated chitosaccharides, one of the artefacts (*A*) was isolated crystalline in very low yield. Analysis suggested that it was derived from 2-acetamido-2-deoxy-D-glucose by loss of water. The strong infrared absorptions at 1637 and 1545 cm.$^{-1}$ indicated that the acetamido-group was intact. In these respects and in R_F value (in water-saturated butan-1-ol), the product *A* resembles chromogen I isolated by Kuhn and Krüger [8] from a mixture of three chromogens (believed to be those involved in the Morgan–Elson test [9,10]) obtained by treatment of 2-acetamido-2-deoxy-D-glucose with a strongly basic resin or barium hydroxide at 90° or by treatment of 2-amino-2-deoxy-D-glucose penta-acetate with barium methoxide at room temperature. Chromogen I, which has not been obtained crystalline and is probably formed by dehydration of 2-acetamido-2-deoxy-D-glucofuranose,[8] reacts strongly with *p*-dimethylaminobenzaldehyde (Ehrlich's reagent) in acid solution to yield an intense colour with absorption maxima at 512 (weak), 542, and 584 mμ. Under the same conditions product *A* gave only a weak fading colour but after treatment with alkali, as in the Morgan–Elson test, and subsequent reaction with Ehrlich's reagent an intense colour was produced with absorption maxima at 512 (weak), 543, and 582 mμ, similar to that given by chromogen I. Chromogen I showed weak absorption at 230 mμ, whereas product *A* showed no maximal absorption in the range 210—260 mμ, and, further, the affinities of the two compounds for charcoal–Celite were different: chromogen I was eluted only with >15% aqueous alcohol (*i.e.*, 15% ethanol v/v) whereas product *A* was eluted with 5%. Although the structural relations between product *A* and chromogen I cannot be precisely defined the former is possibly the precursor of the latter.

Chitin is de-*N*-acetylated by solid potassium hydroxide at 170—190° under nitrogen.[11] The product, chitosan, usually isolated as a water-soluble salt which still contains *N*-acetyl residues, is more amenable to controlled fragmentation than chitin itself. Chitosan

[6] Bergmann, Zervas, and Silberkweit, *Ber.*, 1931, **64**, 2436.
[7] Whistler and Durso, *J. Amer. Chem. Soc.*, 1950, **72**, 677.
[8] Kuhn and Krüger, *Chem. Ber.*, 1956, **89**, 1473; 1957, **90**, 264.
[9] Morgan and Elson, *Biochem. J.*, 1934, **28**, 988.
[10] Aminoff, Morgan, and Watkins, *ibid.*, 1952, **51**, 379.
[11] Ricketts, *Research*, 1953, **6**, 17-S, and personal communication.

exhibits remarkable resistance towards acidic hydrolysis, owing to electrostatic shielding [12] of the polysaccharide chains by the NH_3^+ groups which prevents the approach of hydrions; it was not completely hydrolysed by treatment with 3·3N-hydrochloric acid at 100° for 3 days. After 32 hours' treatment it was converted into a series of chitosaccharides, but because of the low affinity for the absorbent attempts to fractionate the mixture on charcoal–Celite were unsuccessful. However, selective *N*-acetylation [13] of the chitosaccharide mixture followed by chromatography on charcoal–Celite gave the first seven members of a saccharide series of which the first five were obtained crystalline, and the tri- and higher saccharides were hitherto unknown. Table 1 shows the fractions obtained and related data.

Several lines of evidence suggest that the *N*-acetylchitosaccharides are members of a

TABLE 1. *Data on the* N-*acetylated chitosaccharides.*[a]

Fraction [b]	Alcohol (% v/v) in eluate	Saccharide component	No. of monosacch. units	R_{Ac} [c]	Yield [d] (g.)	$[M]_D$
I	2·8—5·0	2-Acetamido-2-deoxy-D-glucose	1	1·00	2·75	+90°
II	10·0—11·6	Di-*N*-acetylchitobiose	2	0·89	1·11	+73
III	15·9—19·1	Tri-*N*-acetylchitotriose	3	0·71	1·20	+14
IV	21·0—23·0	Tetra-*N*-acetylchitotetraose	4	0·60	0·81	−34
V	24·0—26·4	Penta-*N*-acetylchitopentaose	5	0·30	0·70	−94
VI	26·8—28·6	Hexa-*N*-acetylchitohexaose	6	0·10	0·43	−141
VII	29·3—30·1	Hepta-*N*-acetylchitoheptaose	7	0·03	0·09	−181

		Found				Required			
Fraction [b]	Formula	C%	H%	N%	*M* [e]	C%	H%	N%	*M*
I	$C_8H_{15}O_6N$	43·6	6·95	6·3	208	43·4	6·8	6·3	221
II	$C_{16}H_{28}O_{11}N_2$	45·1	6·9	6·6	420	45·3	6·6	6·6	424
III	$C_{24}H_{41}O_{16}N_3$	45·7	6·5	6·2	652	45·9	6·5	6·7	627
IV	$C_{32}H_{54}O_{21}N_4$	46·0	6·7	6·8	871	46·3	6·5	6·75	830
V	$C_{40}H_{67}O_{26}N_5$	46·6	6·5	6·05	1050	46·5	6·5	6·8	1033
VI	$C_{48}H_{80}O_{31}N_6$	—	—	—	1225	—	—	—	1236
VII	$C_{56}H_{93}O_{36}N_7$	—	—	—	1317	—	—	—	1439

[a] Obtained by fractionation of a mixture (10·16 g.) on a charcoal–Celite column [7] (420 × 55 mm.) by gradient elution [14] with aqueous ethanol. [b] Intermediate fractions were obtained which contained more than one component. [c] Obtained with pyridine–pentan-2-ol–water as solvent.[15] [d] Total recovery from the column was 86%. [e] Values determined in aqueous solutions.

polymer-homologous series. Thus a plot of $[M]_D/n$ against $(n - 1)/n$, where $[M]_D$ is the molecular rotation and n is the degree of polymerisation (D.P.), yielded a straight line (Fig. 1). Freudenberg *et al.*[16] predicted this result for a homologous series of oligosaccharides when $n > 1$. The change in the sign of $[M]_D$ from positive to negative as n increases indicates β-linkages.

It has been shown [17] that a plot of log $(1/R_F - 1)$ against n, where R_F is the paper-chromatographic mobility and n is the D.P., yields a straight line for a homologous series of oligosaccharides. This relation was observed (Fig. 2) for the R_F values of the *N*-acetylated chitosaccharides obtained with the organic phase of butanol–ethanol–water–ammonia (40 : 49 : 10 : 1). However a plot of the R_F values obtained with pyridine–pentan-2-ol–water [15] (1 : 1 : 1) yielded a smooth curve (Fig. 3), as did the R_F values similarly obtained for the cellosaccharides (Fig. 3). In contrast, a straight-line

[11] Cf. Foster and Huggard, *Adv. Carbohydrate Chem.*, 1955, **10**, 335, and references cited therein.
[13] Roseman and Ludowieg, *J. Amer. Chem. Soc.*, 1954, **76**, 301.
[14] Lindberg and Wickberg, *Acta Chem. Scand.*, 1954, **8**, 569.
[15] Jeanes, Wise, and Dimler, *Analyt. Chem.*, 1951, **23**, 415.
[16] Freudenberg, Friedrich, and Bumann, *Annalen*, 1932, **494**, 41; cf. Whelan, Bailey, and Roberts, *J.*, 1953, 1294; Wolfrom and Dacons, *J. Amer. Chem. Soc.*, 1952, **74**, 5331; Whistler and Chen-Chuan Tu, *ibid.*, p. 3609.
[17] French and Wild, *ibid.*, 1953, **75**, 2612; cf. Martin, *Biochem. Soc. Symp.*, 1949, **3**, 4; Bate-Smith and Westhall, *Biochim. Biophys. Acta*, 1950, **4**, 427; also ref. 15.

plot was obtained with the R_F values obtained for the maltosaccharides (Fig. 3). The similarity in chromatographic behaviour of the *N*-acetylchitosaccharides and the cellosaccharides is striking and the smooth curves obtained indicate the homologous nature of the oligosaccharide series.

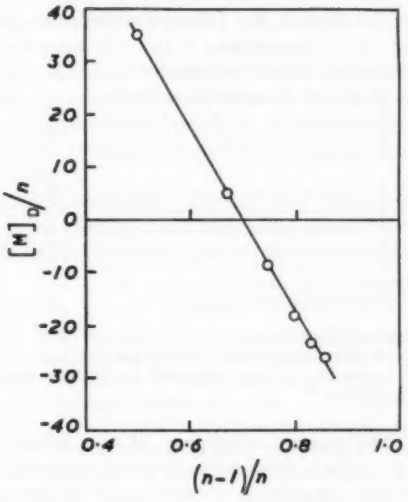


FIG. 1. *Relation between* $[M]_D/n$ *and* $(n-1)/n$ *for* N-*acetylchitosaccharides, where* n = *no. of monosaccharide units.*

FIG. 2.

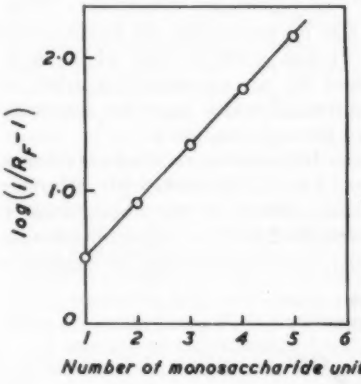
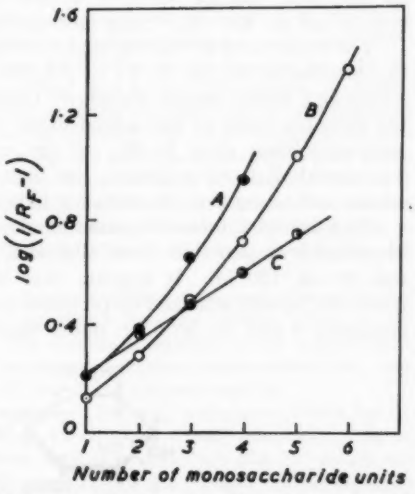


FIG. 3.



Relation between $\log(1/R_F-1)$ *and* n: FIG. 2, N-*acetylchitosaccharides,* R_F *values being determined with the organic phase of butanol–ethanol–water–ammonia* (40 : 10 : 49 : 1); FIG. 3, N-*acetylchitosaccharides* (*A*), *cellosaccharides* (*B*), *and maltosaccharides* (*C*), R_F *values being determined with pyridine–pentan-2-ol–water.*[15]

Infrared-spectral data for the *N*-acetylchitosaccharides and related compounds are shown in Table 2. All the *N*-acetylchitosaccharides and chitin show absorption at 884—900 cm.$^{-1}$ (type 2b) indicative[18] of β-glucopyranosidic linkages, whereas only the

crystalline forms of 2-acetamido-2-deoxy-D-glucose, di-*N*-acetylchitobiose, and tri-*N*-acetylchitotriose showed absorptions at *ca.* 850 cm.$^{-1}$ (type 2a) indicative [18] of α-glucopyranose derivatives. That these saccharides crystallise in the α-form is suggested by the downward mutarotation exhibited in each case on dissolution in water.

TABLE 2. *Infrared absorptions of chitosaccharides and related compounds*

Compound	State [a]	Frequencies [b]					
2-Acetamido-2-deoxy-α-D-glucose [c] ...	X	—	933w	909m	884m	850m	770m
No. of units in N-acetylchitosaccharides:							
2	X	966w	947m	905m	892w	840m	—
2	f.d.	961m	947m	—	896m	—	—
3	X	961m	947m	917w	899m, 888m	857w	—
3	f.d.	—	945m	—	892m	—	—
4	f.d.	—	951m	—	892m	—	—
5	f.d.	—	951m	—	894m	—	—
6	f.d.	—	955m	—	900m	850vvw	—
7	f.d.	—	950m	—	900m	860vvw	—
Chitin [d]	—	970m	947m	—	888m	—	—
2-Acetamido-2-deoxy-D-glucitol	X	966m	939m	—	892m, 876s	—	761wb
Di-*N*-acetylchitobi-itol	f.d.	—	942m	—	892m	—	—

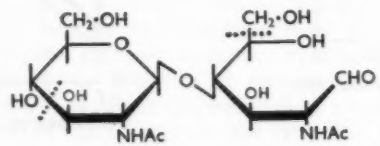
[a] X = crystalline; f.d. = freeze-dried. [b] w = weak; m = medium; s = strong; v = very; b = broad. [c] Data recorded by Barker *et al.*[18] [d] Sample prepared as described by Foster and Hackman.[19]

The general similarity of the infrared spectra of the *N*-acetylchitosaccharides of D.P. >2 was most noticeable and suggested a close structural relation.

The absorption at 892 cm.$^{-1}$ in the spectrum of di-*N*-acetylchitobi-itol cannot be considered diagnostic of a β-linkage since 2-acetamido-2-deoxy-D-glucitol, which contains no glycosidic linkage, absorbs in this range. However, the absence of absorption of type 2a (at *ca.* 850 cm.$^{-1}$) may be regarded as negative evidence in favour of a β-linkage.

The response of acetamido-sugars to the Morgan–Elson test [10] is significantly influenced by substitution of the 3-, 4-, or 6-hydroxyl group.[20] In particular, substitution of the 4-hydroxyl group largely eliminates response to the test by preventing the formation of the furanose form of the amino-sugar derivative.[8] It was observed that whilst di-*N*-acetylchitobiose gave 3—6% of the colour produced by an equimolar quantity of 2-acetamido-2-deoxy-D-glucose the higher *N*-acetylchitosaccharides gave no detectable colour, indicating that the reducing moieties are linked through position 4.

Di-*N*-acetylchitobiose in unbuffered solution at room temperature reduced only 1 mol. of sodium metaperiodate in *ca.* 4 hr. and, with release of 1 mol. of formaldehyde, a further mol. in *ca.* 120 hr. It appears that the non-reducing moiety of the disaccharide is relatively rapidly attacked by periodate (methyl 2-acetamido-2-deoxy-α-D-glucopyranoside consumes 1 mol. in *ca.* 5 hr. under similar conditions). The second mol. of oxidant is



(I)

consumed as the *aldehydo*-form of the reducing moiety is attacked (cf. I). The slow reaction indicates the presence of a small proportion of the *aldehydo*-form in equilibrium with the pyranose form (the furanose form is precluded), which accords with the general theory of the composition of the equilibria of the reducing forms of sugars in aqueous

[18] Barker, Bourne, Stacey, and Whiffen, *J.*, 1954, 171.
[19] Foster and Hackman, *Nature*, 1957, **180**, 40.
[20] Jeanloz and Trémège, *Fed. Proc.*, 1956, **15**, 282.

solution.[21] Similar results were observed with tri-*N*-acetylchitotriose. Slow overoxidation occurred with both di-*N*-acetylchitobiose and tri-*N*-acetylchitotriose.

Sodium borohydride readily reduced di-*N*-acetylchitobiose and tri-*N*-acetylchitotriose to, respectively, di-*N*-acetylchitobi-itol and tri-*N*-acetylchitotri-itol. The former alcohol rapidly (<10 min.) consumed *ca.* 1 mol. of periodate and released *ca.* 1 mol. of formaldehyde; a second mol. was consumed relatively slowly (*ca.* 11 hr.). Rapid attack at the acyclic moiety would be expected from both known data [22] and the observed rapid reaction of 2-acetamido-2-deoxy-D-glucitol with periodate. Similarly tri-*N*-acetylchitotri-itol rapidly (<10 min.) consumed *ca.* 1 mol. of periodate and released *ca.* 1 mol. of formaldehyde, and slowly (*ca.* 24 hr.) consumed a second mol. of oxidant; acidic hydrolysis of the product formed on complete oxidation released 2-amino-2-deoxy-D-glucose, presumably from the central moiety of the molecule.

The optical rotations, infrared spectra, periodate oxidation patterns, and colorimetric tests described for di-*N*-acetylchitobiose and its reduced derivative substantiate the β1 ⟶ 4 linkage previously allocated to the disaccharide on the basis of other evidence.[6,23]

Experimental

Isolation of Chitin.—Cleaned and fragmented shells of the common edible crab, *Cancer pagurus*, were twice digested overnight at room temperature with excess of 2N-hydrochloric acid. After being washed free from acid the shells were dried at 100° and then ground in a ball-mill (steel balls) until most of the product passed through a 60-mesh sieve.

Crude powdered chitin (490 g.) was suspended in 2N-hydrochloric acid for 48 hr., then collected by centrifugation, washed with water, and extracted with aqueous sodium hydroxide (2 l.; 5% w/v) for 12 hr. at 100°. The product was isolated from the hot suspension by centrifugation and the alkaline extraction repeated four times. The final residue was freed from alkali by washing with water, neutralisation with hydrochloric acid, and prolonged dialysis against water. After drying, the chitin (277 g.) was obtained as a straw-coloured powder [Found: C, 44·6; H, 6·4; N, 6·2. Calc. for $(C_8H_{13}O_5N)_n$: C, 47·3; H, 6·4; N, 6·9%].

Acetolyses of Chitin.—(*a*) Chitin (10 g.) was added to a cooled mixture of acetic anhydride (50 ml.) and concentrated sulphuric acid (6·5 ml.). After storage at room temperature for 40 hr. and then at 55° for 11 hr. the mixture was added to a cooled (0°) solution of sodium acetate trihydrate (40 g.) in water (260 ml.). Insoluble material was removed by centrifugation and, after several hours, the supernatant liquid was neutralised with solid sodium carbonate and extracted with chloroform (3 × 200 ml.). The combined extracts were washed with water, dried (Na_2SO_4), and concentrated, and the residue was triturated with methanol. Recrystallisation of the crude product (3 g.) from methanol gave chitobiose octa-actate as colourless needles (1·14 g.), m. p. 286—288°. A second recrystallisation gave the product (0·2 g.), m. p. 308—309° (decomp.), $[M]_D^{18}$ +372° (*c* 0·5 in acetic acid) (Found: C, 49·4; H, 5·9; N, 4·3. Calc. for $C_{28}H_{40}O_{17}N_2$: C, 49·7; H, 5·9; N, 4·1%).

(*b*) Chitin (125 g.) was acetolysed in several portions as described in (*a*) and, after neutralisation, the insoluble material was extracted with chloroform and the extract added to the chloroform extract of the supernatant liquor. The combined extracts were washed with water, dried (Na_2SO_4), and concentrated and the residue was triturated with methanol to yield, after drying *in vacuo* (P_2O_5), a mixture (17·46 g.) of acetylated chitosaccharides.

A solution of this material (16·1 g.) in dry methanol (700 ml.) was deacetylated by the addition of a trace of metallic sodium [α_D (2 dm. tube) +0·09° ⟶ +0·65° (constant)]. After 40 hr. the solution was diluted with water, freed from cations by Zeo-Carb 225 (H^+ form), and evaporated under diminished pressure, to yield the product (9·9 g.). Paper chromatography with the organic phase of butanol–ethanol–water–ammonia (40 : 10 : 49 : 1) and detection with aniline hydrogen phthalate [24] and alkaline silver nitrate [25] revealed five components with R_{Ac} values (mobility relative to that of 2-acetamido-2-deoxy-D-glucose) 0·24, 0·52, 0·78, 1·00, and 1·87.

[21] See Pigman, "The Carbohydrates," Academic Press, New York, 1957, p. 54.
[22] Bobbitt, *Adv. Carbohydrate Chem.*, 1956, **11**, 1.
[23] Zechmeister and Tóth, *Enzymologia*, 1939, **7**, 165.
[24] Partridge, *Nature*, 1949, **164**, 443.
[25] Trevelyan, Proctor, and Harrison, *ibid.*, 1950, **166**, 444.

A solution of the mixed products (10·4 g.) in water (100 ml.) was introduced on to a charcoal–Celite column [7] (400 × 57 mm.), and eluted successively with water (4 l.) and aqueous ethanol of ethanol concentrations (v/v) 2·5% (5 l.), 5% (14 l.), 7·5% (15·5 l.), 10% (13 l.), and 15% (5·5 l.); 86% of the original mixture was thus eluted. In this and similar column separations up to eleven products, R_{Ac} 0·11—2·73, could be detected on analysis of the 50 ml. fractions collected. The principal fractions are recorded in Table 3

TABLE 3.

Fraction	Vol. of eluate (l.)	Main component (R_{Ac} value)	Yield (g.)
I	3—7·5	2-Acetamido-2-deoxy-D-glucose (1·00†)	0·48
II	10·5—24·5	Di-*N*-acetylchitobiose (0·52)	5·54
III	42·5—49·5	Tri-*N*-acetylchitotriose (0·24)	1·22

A solution of fraction II (5·2 g.) in water (50 ml.) was introduced on to a charcoal–Celite column [7] (370 × 57 mm.) and the column subjected to gradient elution [14] with aqueous alcohol; the alcohol concentration was increased at the rate of 1·67% per litre. The di-*N*-acetylchitobiose emerged from the column, together with other components, in the eluate range 8·75—11·4 l. Concentration of the fraction 10·15—10·6 l. containing di-*N*-acetylchitobiose together with traces of two other components gave a product (2·69 g.) which, after crystallisation from aqueous methanol, gave the biose [2-acetamido 4-*O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-2-deoxy-D-glucose] as colourless needles (1·71 g.), m. p. 260—262° (decomp.), $[\alpha]_D$ +25·2° (3 min.) ⟶ +17·2° (equilibrium), $[M]_D$ +73° (*c* 0·5 in H_2O). The disaccharide contained *ca.* 0·23% of incombustible material. The analytical data are recorded in Table 1.

Recrystallisation of fraction III (0·4 g.) from aqueous methanol gave tri-*N*-acetylchitotriose (0·2 g.) as microscopic, colourless needles, m. p. 304—306° (decomp.), $[\alpha]_D$ +3·8 (13 min.) ⟶ +2·2° (equil.), $[M]_D$ +14° (*c* 0·9 in H_2O).

In a separate experiment a crude mixture (24 g.) of deacetylated products, obtained as in (*b*), was dissolved in water (250 ml.) and introduced on a charcoal–Celite column [7] (210 × 50 mm.). Elution was initially with water (3 l.) and later with aqueous ethanol, the concentration of ethanol increasing at the rate of 5% per l. for 6 l. and at 10% per l. for the next 3 l. Concentration of the eluate fraction 5·1—5·25 l. gave a product (0·18 g.) which contained several components. Crystallisation from dry methanol gave *compound A* (37 mg.), m. p. 175—177° (Found: C, 46·8; H, 6·4; N, 6·8. $C_8H_{13}O_5N$ requires C, 47·3; H, 6·4; N, 6·9%). This reacted strongly, on paper chromatograms, with aniline hydrogen phthalate, and with the organic phase of butanol–ethanol–water–ammonia (40 : 10 : 49 : 1) had R_{Ac} 1·87.

De-N-acetylation of Chitin.—Chitin (21 g.; H_2O content 6·7%) and potassium hydroxide (40 g.) were heated together at 170—190° in a current of nitrogen for 95 min. The cooled mixture was treated with water (250 ml.) and concentrated hydrochloric acid (64 ml.). After dialysis of the product against running tap water for 42 hr. and against distilled water for 5 hr., insoluble material (3 g.) was removed by centrifugation and the supernatant liquid concentrated by freeze-drying, to yield chitosan hydrochloride (11·4 g.) [Found: Cl, 13·1. Calc. for $(C_6H_{12}O_4NCl)_n$: Cl, 17·95%]. The chloride content of the chitosan hydrochloride could not be determined by direct precipitation of silver chloride since the salt failed to coagulate and precipitate in the presence of the polysaccharide. The following procedure proved to be satisfactory: Chitosan hydrochloride (0·4 g.) was suspended in 0·225N-sulphuric acid (37 ml.) and treated with 2·76% w/v aqueous sodium nitrite (37 ml.) at room temperature for 45 min. Silver chloride was then precipitated and determined by the usual method. A control experiment was performed on 2-amino-2-deoxy-D-glucose hydrochloride (Found: Cl, 16·3. Calc. for $C_6H_{14}O_5NCl$: Cl, 16·5%).

Acidic Hydrolysis of Chitosan Hydrochloride.—The following conditions appeared to be optimum for the production of a series of oligosaccharides. A solution of chitosan hydrochloride (3·1 g.) in water (210 ml.) was heated to 100° and concentrated hydrochloric acid (90 ml.) added. The solution was kept at 100° for 34 hr., then cooled, decolorised with activated charcoal, and neutralised with methyldi-*n*-octylamine.[26] Paper chromatography of the hydrolysate with pyridine–pentan-2-ol–water (1 : 1 : 1) as solvent [15] and detection with aniline hydrogen phthalate [24] or ninhydrin revealed the presence of mono- to hexa-saccharide. Attempts to fractionate the mixture on charcoal–Celite [7] failed because it was too weakly absorbed and was eluted by water.

[24] Smith and Page, *J. Soc. Chem. Ind.*, 1948, **67**, 48.

XUM

A solution of the saccharide mixture (2·97 g.) in water (75 ml.) was treated at 0° with methanol (7·5 ml.), Amberlite IRA-400 (CO_3^{2-} form; 90 ml.) and acetic anhydride (2 ml.); the stirred mixture was stored at 0—5° for 1·5 hr. Thereafter the resin was removed and replaced by Amberlite IR-120 (H^+ form, 4 ml.) in order to remove any free amino-sugars. The de-ionised solution was concentrated to 50 ml., insoluble material (0·46 g.) was removed by centrifugation, and the supernatant liquid concentrated by freeze-drying to yield a mixture (1·96 g.) of *N*-acetylchitosaccharides. Paper chromatography of the *N*-acetylchitosaccharide mixture with pyridine–pentan-2-ol–water [15] and detection with alkaline silver nitrate [25] revealed a series of at least six components with R_{Ac} <1·0 and a small amount of a component of R_{Ac} 1·2.

A similar *N*-acetylchitosaccharide mixture (10·16 g.), dissolved in water (110 ml.), was introduced on to a charcoal–Celite column [7] (420 × 55 mm.) and submitted to gradient elution with aqueous ethanol; the ethanol concentration increased at the rate of 1·67% per l. The fractions which contained pure components are recorded in Table 1 together with other data.

Crystallisation of fractions III (0·9 g.), IV (0·69 g.), and V (0·68 g.) from aqueous methanol gave respectively: tri-*N*-acetylchitotriose (0·63 g.), m. p. 309—311° (decomp.), $[\alpha]_D^{17}$ +2·5° ± 0·4° (equil.; *c* 1·2 in H_2O), $[M]_D$ +16°, *tetra*-N-*acetylchitotetraose* (0·39 g.), m. p. 290—300° (decomp.), $[\alpha]_D^{20}$ −4·1° ± 0·2°, (equil.; *c* 1·0 in H_2O), $[M]_D$ −34°, and *penta*-N-*acetylchitopentaose* (0·3 g.), m. p. 285—295° (decomp.), $[\alpha]_D^{20}$ −9·1° ± 0·2° (equil.; *c* 1·0 in H_2O), $[M]_D$ −94°, all small colourless needles.

All the *N*-acetylchitosaccharides, before crystallisation, contained significant amounts of incombustible material which was considerably reduced but not eliminated after crystallisation. Hexa-*N*-acetylchitohexaose, $[\alpha]_D$ −11·4° ± 0·4° (equil.; *c* 0·8 in H_2O), $[M]_D$ −141°, and hepta-*N*-acetylchitoheptaose, $[\alpha]_D$ −12·6° ± 1·9° (equil.; *c* 0·3 in H_2O), $[M]_D$ −181°, were not obtained crystalline; both appeared homogeneous on paper chromatography. Analytical and other data for these saccharides are recorded in Table 1.

Acetylation of Tri-N-acetylchitotriose.—The trisaccharide (0·25 g.) was treated with acetic anhydride (2·5 ml.) and pyridine (2·5 ml.) at room temperature for 2 days. Insoluble material was collected by centrifugation and re-treated with the reagents. The combined reaction mixtures were freed from insoluble material by centrifugation and diluted with ice-water (125 ml.). The solution was extracted with chloroform (3 × 30 ml.), the combined extracts were washed successively with water, aqueous sodium hydrogen carbonate, and water, then dried (Na_2SO_4), and concentrated. Recrystallisation of the residue gave *chitotriose hendecaacetate* (50 mg.) as colourless needles, m. p. 304—305° (decomp.), $[\alpha]_D^{18}$ +30° ± 2° (*c* 0·5 in acetic acid) (Found: C, 49·6; H, 5·8; N, 4·3. $C_{46}H_{67}O_{34}N_3$ requires C, 49·8; H, 5·9; N, 4·4%).

Hypoiodite Oxidation of the N-Acetylated Chitosaccharides.[27]—Preliminary experiments revealed that overoxidation of 2-acetamido-2-deoxy-D-glucose occurred if the reaction was performed at room temperature. All oxidations were therefore carried out at 0°.

Samples of the *N*-acetylchitosaccharides in Table 2 (1·5, 1·0, and 0·67 mg.) were separately dissolved in water (*ca.* 0·5 ml.) and treated successively with a mixture (1 ml. containing equal parts by volume of 0·2M-sodium carbonate and 0·2M-sodium hydrogen carbonate) and 0·02N-iodine (1 ml.). The reaction solutions were stored at 0—2° for 18 hr., then acidified with 5N-sulphuric acid (10 ml.), diluted with water (*ca.* 10 ml.), and titrated with standard thiosulphate solution. The results (average of three determinations) are recorded in Table 1.

Behaviour of the N-Acetylated Chitosaccharides in the Morgan–Elson Test.—Samples (1 ml.) of aqueous solutions (containing *ca.* 100 μg./ml.) of the saccharides in Table 2 and 2-acetamido-2-deoxy-D-glucose (containing 100, 70, and 40 μg./ml.) were treated with sodium carbonate and *p*-dimethylaminobenzaldehyde as described by Aminoff, Morgan, and Watkins.[19] The colour which developed was measured with a Spekker photoelectric absorptiometer with Ilford No. 605 filters.

No detectable colour was produced by tri-*N*-acetylchitotriose and the higher saccharides, but di-*N*-acetylchitobiose gave *ca.* 3—6% of the colour produced by an equimolar amount of the monosaccharide.

Reduction of Di-N-acetylchitobiose.—A solution of this biose (0·4 g.) in water (12 ml.) was treated with sodium borohydride (31 mg.) in water (4 ml.) at room temperature for 2·5 hr. (In preliminary experiments the reaction was followed polarimetrically and shown to be essentially complete within 60 min.) Dilute acetic acid was then added dropwise until excess

[27] Cf. Jeanloz and Forchielli, *Helv. Chim. Acta*, 1950, **33**, 1690.

of borohydride was decomposed, and the solution was de-ionised by Amberlite resins IR-120 (H^+ form; 4 ml.) and IRA-400 (HO^- form; 4 ml.). Concentration of the solution gave a solid residue (0·38 g.) which appeared homogeneous on paper chromatography. Recrystallisation from ethanol gave *di-N-acetylchitobi-itol* [*2-acetamido-4-O-(2-acetamido-2-deoxy-β-D-gluco-pyranosyl)-2-deoxy-D-glucitol*] *monohydrate* as extremely hygroscopic large colourless plates (0·22 g.), m. p. 102—105°, $[M]_D$ −51° (*c* 1·6 in H_2O) (Found: C, 43·2; H, 7·1; N, 6·4. $C_{16}H_{30}O_{11}N_2,H_2O$ requires C, 43·2; H, 7·2; N, 6·3%). A sample, dried to constant weight *in vacuo* at 60° over phosphoric oxide, lost 4% of its weight when the temperature was raised to 130° (Calc.: H_2O, 4·05%).

Reduction of Tri-N-acetylchitotriose.—The trisaccharide (0·4 g.) was reduced as for the disaccharide, to yield a product (0·35 g.) which on crystallisation from ethanol gave *tri-N-acetylchitotri-itol* as very hygroscopic colourless needles (0·15 g.), m. p. 195—200°, $[M]_D$ −64° (*c* 1·0 in H_2O) (Found: C, 45·5; H, 7·0; N, 6·5. $C_{24}H_{43}O_{16}N_3$ requires C, 45·8; H, 6·8; N, 6·7%)

Periodate Oxidations.—The following general procedure was adopted. A solution of the substrate (*ca.* 0·13 mmole) in water (*ca.* 25 ml.) was treated with 0·25M-sodium metaperiodate (15 or 5 ml.), and the volume rapidly adjusted to 50 ml. The consumption of periodate was determined on aliquot parts by the standard arsenite method. The blue colour produced at the end-point when using Thyodene (starch–urea mixture) as indicator, faded rapidly in the analysis of samples withdrawn after *ca.* 2 hr. The effect, which presumably is due to some form of overoxidation, could be minimised by performing titrations at <10°.

Acidity which developed in the solutions was determined in aliquot parts, after destruction of excess of periodate with ethylene glycol, by titration with standard alkali. Formaldehyde was determined by the chromotropic acid method.[28]

The following results were obtained at room temperature (12—18°):

(*a*) 2-Acetamido-2-deoxy-D-glucose (0·005106M) in sodium metaperiodate (0·075M):

Time (hr.)	0·1	0·25	0·5	1·0	3·0	6·0	21
Oxidant consumption (mol.)	2·11	2·90	3·66	4·55	4·88	4·96	5·23

After 25 hr. acidity corresponding to 2·16 mols. of formic acid was developed.

(*b*) Di-*N*-acetylchitobiose (0·002604M) in sodium metaperiodate (0·075M):

Time (hr.)	1	4	23	44	92	140	188	260
Oxidant consumption (mol.)	—	1·04	1·55	1·78	1·93	2·07	2·16	2·37
Formaldehyde liberation (mol.)	0·09	0·18	0·55	0·72	0·91	0·97	0·97	—

After 140 hr. acidity corresponding to 0·08 mol. of formic acid had developed.

(*c*) Tri-*N*-acetylchitotriose (0·002632M) in sodium metaperiodate (0·075M):

Time (hr.)	3	24	50	72	120	168
Oxidant consumption (mol.)	1·05	1·81	2·15	2·19	2·24	2·38
Formaldehyde liberation (mol.)	0·20	0·77	0·96	1·02	1·03	1·03

Development of acidity (as mol. of formic acid) in 72 hr. was 0·08 mol., and in 216 hr. 0·30 mol.

(*d*) 2-Acetamido-2-deoxy-D-glucitol (0·002664M) in sodium metaperiodate (0·025M):

Time (hr.)	0·25	1·0	20
Oxidant consumption (mol.)	2·96	3·00	3·00
Formaldehyde	1·01	1·01	1·01

(*e*) Methyl 2-acetamido-2-deoxy-α-D-glucopyranoside (0·002596M) in sodium metaperiodate (0·025M):

Time (hr.)	0·2	0·5	1·0	2·0	4·25	21	30
Oxidant consumption (mol.)	0·19	0·34	0·49	0·68	0·89	1·02	1·02

(*f*) Di-*N*-acetylchitobi-itol (0·002624M) in sodium metaperiodate (0·025M):

Time (hr.)	0·16	1·0	3·0	5·75	11·0	24	48
Oxidant consumption (mol.)	0·98	1·13	1·40	1·69	1·92	2·07	2·07
Formaldehyde liberation (mol.)	1·07	0·99	1·02	—	—	1·02	—

No formic acid was produced in 48 hr.

(*g*) Tri-*N*-acetylchitotri-itol (0·002652M) in sodium metaperiodate (0·025M):

Time (hr.)	0·16	1·0	3·0	6·0	10·0	24	48
Oxidant consumption (mol.)	0·89	1·04	1·28	1·64	1·79	1·90	1·95
Formaldehyde liberation (mol.)	0·96	0·98	0·98	—	—	0·97	—

No formic acid had been produced in 48 hr.

[28] O'Dea and Gibbons, *Biochem. J.*, 1953, **55**, 580.

The reaction solution (*g*) (5 ml.) after 48 hours was treated with excess of ethylene glycol (0·1 ml.) and, after a few minutes, with a solution of sodium borohydride (5 mg.) in water (1 ml.) at room temperature for 1 hr. After decomposition of the reducing agent with acetic acid the solution was de-ionised with Amberlite resins IR-120 (H^+ form) and IRA-400 (HO^- form) and concentrated to 2 ml. The solution was made 2N with respect to hydrochloric acid, heated at 100° for 2 hr., neutralised with methyldi-*n*-octylamine and subjected to ionophoresis (neutral buffer). A component was present with behaviour identical with that of 2-amino-2-deoxy-D-glucose.

Infrared Spectra.—Infrared spectra were measured by the potassium bromide disc method with a Grubb-Parsons single-beam spectrometer.

The authors thank Dr. D. H. Whiffen for advice on the infrared spectra. One of them (J. M. W.) thanks the D.S.I.R. for a maintenance award.

CHEMISTRY DEPARTMENT, THE UNIVERSITY,
EDGBASTON, BIRMINGHAM, 15. [*Received, December 30th*, 1957.]

---

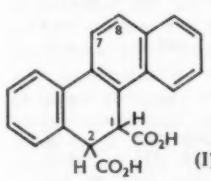
452. *Metallation and Carboxylation of Chrysene.*

By S. E. HUNT and A. S. LINDSEY.

Carboxylation of the chrysene–sodium adduct leads to 1 : 2-dihydrochrysene-1 : 2-dicarboxylic acid. Oxidation of the diacid yields 1 : 2-chrysoquinone, and of the derived anhydride yields chrysene-1 : 2-dicarboxylic anhydride. Treatment of the chrysene–sodium adduct with ethanol gives 1 : 2-dihydrochrysene. The stereochemistry and ultraviolet absorption spectra of the products are discussed.

THE addition of alkali metals to chrysene in complex-forming or co-ordinating solvents has not hitherto been examined in detail. Mohler and Sorge [1] prepared crystalline dihydrochrysene by treatment of chrysene with lithium in diethyl ether followed by ethanol, but no structure was indicated. The theoretical aspects of this type of addition of alkali metals have been discussed by Paul *et al.*[2] and by Ubbelohde and his colleagues.[3] Chrysene and sodium have now been found to form readily an adduct when stirred together in dimethoxyethane at room temperature, the adduct being deposited as an almost black solid. Carboxylation of the suspended sodio-derivative at about −65° gave a crystalline dihydrochrysenedicarboxylic acid.

The carboxylation product was shown to be 1 : 2-dihydrochrysene-1 : 2-dicarboxylic acid (I) by the analytical data, equivalent-weight determination, and infrared absorption spectrum. With diazomethane it gave a crystalline dimethyl ester. At the melting point (280°) or in hot acetic anhydride it was readily converted into an anhydride which on hydrolysis at room temperature and acidification at 0° yielded a dicarboxylic acid which appeared to differ from the starting material in becoming orange-coloured on storage, possibly owing to aerial oxidation but with diazomethane gave the same dimethyl ester. With chromium trioxide in acetic acid the anhydride furnished the orange crystalline chrysene-1 : 2-dicarboxylic anhydride. Oxidation of the dihydrochrochrysenedicarboxylic acid with potassium dichromate yielded 1 : 2-chrysoquinone as sole product.



(I)

Oxidation of chrysene occurs readily at the 1- and the 2-position, and bromination at positions 2 and 8. Bond-order calculations [4] agree with the experimental data. Since with other aromatic systems an alkali metal adds to the most reactive positions it seems

[1] Mohler and Sorge, *Helv. Chim. Acta*, 1939, **22**, 229.
[2] Paul, Lipkin, and Weissman, *J. Amer. Chem. Soc.*, 1956, **78**, 116.
[3] Holmes-Walker and Ubbelohde, *J.*, 1954, 720; Slough and Ubbelohde, *J.*, 1957, 982.
[4] Berthier, Coulson, Greenwood, and Pullman, *Compt. rend.*, 1948, **226**, 1906.

XUM

likely that reaction occurs at the 1 : 2-positions of chrysene in this instance, the vicinal character of the two carboxyl groups being confirmed by the ready anhydride formation. Chrysene-1 : 2-dicarboxylic anhydride was hydrolysed by alkali at room temperature to the very unstable 1 : 2-dicarboxylic acid: the initially pale yellow precipitate rapidly reverted to the orange anhydride. Phenanthrene-9 : 10-dicarboxylic acid behaves similarly.[5] The instability is even more marked with the chrysene compound since attempts to prepare a dimethyl ester led only to recovery of the anhydride. The instability of the diacid with anhydride formation is markedly different from the properties reported for chrysene-2 : 8-dicarboxylic acid.[6]

Two *cis*- and two *trans*-forms of 1 : 2-dihydrochrysene-1 : 2-dicarboxylic acid are possible but there is insufficient evidence for assignment of a complete configuration. Our acid is probably a *trans*-compound since it is unchanged by concentrated hydrochloric acid at 180°; this is consistent with Jeanes and Adams's observation [5] that phenanthrene yields a *trans*-product.

The dihydro-anhydride is considered to have a *cis*-configuration from its mode of formation. A molecular model shows that a *trans*-anhydride is sterically unlikely and the ultraviolet absorption (see Table) suggests that the molecule is essentially planar. Further the infrared absorption bands (at 1858 and 1771 cm.$^{-1}$) are close to those for succinic anhydride [7] (1866 and 1783 cm.$^{-1}$), and indicate that the anhydride ring is not under undue strain.

Treatment of the chrysene–sodium adduct with ethanol gave a crystalline dihydrochrysene, the m. p. and ultraviolet absorption spectrum of which agreed with those reported by Mohler and Sorge.[1] In view of the carboxylation products derived from the same adduct it appears reasonable to assume that the 1 : 2-dihydrochrysene is obtained.

Ultraviolet absorption spectra.

Chrysene		1 : 2-Dihydrochrysene		1 : 2-Dimethylchrysene [a]		2-Phenylnaphthalene [b]	
λ	log ε	λ	log ε	λ	log ε	λ	log ε
220	4·50	216	4·48	—	—	—	—
241	4·32	—	—	—	—	—	—
257	4·86	255	4·73	—	—	251	4·8
266·5	5·13	264	4·88	274	4·95	272	4·1
281	4·08	282	3·96	—	—	—	—
293	4·07	292—293	4·07	—	—	288	4·1
304	4·10	303	4·15	304	3·96	—	—
317	4·10	316	4·06	323	4·08	—	—

6 : 7 Dihydro-3-methylcholanthrene [b]		1 : 2-Dihydrochrysene-1 : 2-dicarboxylic acid		1 : 2 Dihydrochrysene-1 : 2-dicarboxylic anhydride		Chrysene-1 : 2-dicarboxylic anhydride	
λ	log ε	λ	log ε	λ	log ε	λ	log ε
—	—	216	4·43	216	4·43	222	4·52
—	—	238	4·28	239	4·32	—	—
~263	4·67	—	—	247	4·66	—	—
272	4·7	264	4·81	266	4·77	270	4·91
—	—	293	4·02	293	4·03	—	—
—	—	302	4·09	304	4·08	302—303	4·04
314	4·1	314	4·00	316	4·00	314—315	4·08

[a] Jones, *J. Amer. Chem. Soc.*, 1941, **63**, 313. [b] Fieser and Herschberg, *ibid.*, 1938, **60**, 940.

Brode and Patterson [8] report that comparison of the ultraviolet spectra of 1- and 12-methylchrysene with that of chrysene reveals bathochromic and hypochromic shifts

[5] Jeanes and Adams, *J. Amer. Chem. Soc.*, 1937, **59**, 2608.
[6] Funke, Müller, and Vadasz, *J. prakt. Chem.*, 1936, **144**, 265; Funke and Ristic, *ibid.*, 1936, **146**, 151.
[7] Randall, Fowler, Fuson, and Dangl, "Infrared Determination of Organic Structures," Van Nostrand Co. Inc., New York, 1949, p. 163.
[8] Brode and Patterson, *J. Amer. Chem. Soc.*, 1941, **63**, 3253.

XUM

greater than those observed for the other monomethylchrysenes, owing to steric interference between the 1-hydrogen atom and the 12-methyl group. These differences are more marked in the case of 1 : 2-dimethylchrysene,[9] and a similar effect is shown by chrysene-1 : 2-dicarboxylic anhydride, the spectrum of which is similar to that of 1 : 2-dimethylchrysene. On the other hand the ultraviolet spectra of 1 : 2-dihydrochrysene and its 1 : 2-dicarboxylic acid and anhydride do not greatly differ from that of chrysene itself in the 200—320 mμ region, the most intense band being found about 266 mμ. In the substituted compounds the intensities of the absorption bands are, however, somewhat lower. These results suggest that there is little steric interference by tetrahedrally directed substituents at positions 1 and 2 and this is confirmed by molecular models.

Experimental

Microanalyses were carried out by Miss M. Corner, Mrs. A. Grant, and Mrs. D. Butterworth of this laboratory. Ultraviolet absorption spectra of solutions in EtOH were measured by means of a Unicam S.P. 500 spectrophotometer.

Infrared absorption spectra of solids dispersed in potassium chloride discs were measured on a modified Hilger D 209 double-beam instrument [10] with rock-salt prism; only the strong and the medium-strength bands are reported, these being correct to ± 3 cm.$^{-1}$.

Purification of Chrysene.—A commercially available sample was passed in benzene through a column of decolorising charcoal. Concentration of the eluate gave white leaflets of chrysene, m. p. 255—256 (ultraviolet absorption, see Table), showing blue-violet fluorescence in ultraviolet light superior in this property to a sample refined by zone-melting.

Comparison of Reaction of Chrysene with Sodium in Various Solvents.—A qualitative estimation of this reaction by colour formation was made as follows: Chrysene (100 mg.) was dissolved in 50 ml. portions of dry (i) tetrahydrofuran, (ii) 1 : 2-dimethoxyethane, (iii) diethyl ether. Complete dissolution was achieved with the first two solvents, but only partial in the third, by bubbling dry nitrogen through each solution. A 20% dispersion of sodium in xylene (4 ml.) was added, and the tubes were stoppered and left at room temperature. The observations are summarised.

Time	Dimethoxyethane	Tetrahydrofuran	Diethyl ether
20 min.	Pale green	Colourless	Colourless
18 hr.	Pale green	Slight colour	Colourless
40 hr.	Pale green	Dark green	Colourless
113 hr.	Dark green	Dark green	Colourless

Treatment of the Sodium–Chrysene Addition Compound with Carbon Dioxide.—A suspension of chrysene (20 g.) in 1 : 2-dimethoxyethane (400 ml.) was added to a sodium dispersion (50% of sodium in decalin; 18 ml.) stirred under nitrogen, the temperature being kept at 19—24° by cooling. A deep green colour developed and in 4 hours' stirring the solid product was deposited. The mixture was cooled to −65° and dry carbon dioxide was passed over the stirred mixture for 1·5 hr., during which the green colour became discharged and a yellow suspension was formed. After filtration and washing with benzene, the product was dried in a vacuum-desiccator. Cautious treatment with ice-water and filtration removed unchanged chrysene (7·9 g.). Addition of hydrochloric acid to the filtrate precipitated the crude acid, which was filtered off, washed with water, and dried at 100° (yield 15 g.). Recrystallisation from acetic acid gave the *1 : 2-dihydrochrysene-1 : 2-dicarboxylic acid*, m. p. 280° (decomp.) (Found: C, 75·4, 75·3; H, 4·45, 4·5%; equiv., 161·5. $C_{20}H_{14}O_4$ requires C, 75·5; H, 4·4%; equiv., 159), ν *ca.* 3066, *ca.* 2893, *ca.* 2650, 1732, 1699, 1606, 1410, 1287, 1239, 1225, 1198, 1166, 1149, 812, 762, and 735 cm.$^{-1}$.

Treatment of the acid in methanol–ether with ethereal diazomethane gave the *dimethyl ester* which, recrystallised from light petroleum (b. p. 60—80°), had m. p. 165·5° (Found: C, 76·3; H, 5·2. $C_{22}H_{18}O_4$ requires C, 76·3; H, 5·2%). Hydrolysis of the ester with aqueous-methanolic alkali regenerated the starting material.

Treatment of the Sodium–Chrysene Adduct with Ethanol.—The sodium adduct was prepared from chrysene (8 g.) as described above, and the bulk of the dimethoxyethane removed by

[9] Jones, *J. Amer. Chem. Soc.*, 1941, **63**, 313.
[10] Hales, *J. Sci. Instr.*, 1949, **26**, 359; 1953, **30**, 52.

distillation. Ethanol (100 ml.) was added and the mixture warmed. After cooling, unchanged chrysene (5 g.) was filtered off and concentration of the filtrate gave the dihydrochrysene (2·8 g.), m. p. 171—173° (from ethanol; charcoal) (Found: C, 94·0; H, 5·9. Calc. for $C_{18}H_{14}$: C, 93·9; H, 6·1%), ν 1612, 1484, 1431, 1381, 1270, 1205, 1029, 864, 817, 763, 758, and 734 cm.$^{-1}$.

1 : 2-*Dihydrochrysene*-1 : 2-*dicarboxylic Anhydride*.—(i) Heating 1 : 2-dihydrochrysene-1 : 2-dicarboxylic acid (2 g.) at 280—290° for 2 hr. caused a loss in weight of 0·25 g. The solid product, recrystallised twice from benzene as yellow prisms (1·2 g.), was the *anhydride*, m. p. 251—252° (Found: C, 79·7; H, 4·25. $C_{20}H_{12}O_3$ requires C, 80·0; H, 4·0%), ν 1858, 1771, 1492, 1234, 1205, 1198, 1070, 1038, 1028, 1001, 924, 898, 879, 859, 825, 769, 755, and 716 cm.$^{-1}$.

(ii) The dicarboxylic acid (2 g.) was refluxed with acetic anhydride (50 ml.) for 6 hr. Most of the acetic acid was removed by distillation, the remainder by azeotropic distillation with benzene, to give the solid anhydride, m. p. and mixed m. p. 251—252° (from benzene) (1·35 g.) (Found: C, 80·1; H, 4·2%).

The anhydride (280 mg.) was treated with 10% sodium hydroxide solution (50 ml.) at room temperature for 48 hr. A little insoluble material was filtered off and the solution acidified with dilute hydrochloric acid at 0°. The white precipitate, which was immediately filtered off and washed with water, gradually became buff, had m. p. 267—268° (decomp.) and was orange after being kept overnight [m. p. 250—255° (decomp.)]. The bulk of the precipitate, however, was immediately treated in methanol with ethereal diazomethane. The diester recrystallised from light petroleum (b. p. 80—100°) as prisms, m. p. and mixed m. p. 163—165°.

Dichromate Oxidation of 1 : 2-*Dihydrochrysene*-1 : 2-*dicarboxylic Acid*.—To the acid (1·35 g.) in refluxing acetic acid (50 ml.) was added portionwise solid potassium dichromate (7 g.). After 1 hr. part of the acid was distilled off and the residue poured into ice-water. The precipitated solid (0·75 g.) was recrystallised from acetone (m. p. 237—238°) and was shown to be 1 : 2-chrysoquinone by comparison with an authentic specimen (mixed m. p. and infrared spectrum) (Found: C, 83·6; H, 3·8. Calc. for $C_{18}H_{10}O_2$: C, 83·7; H, 3·9%).

Chromium Trioxide Oxidation of 1 : 2-*Dihydrochrysene*-1 : 2-*dicarboxylic Anhydride*.—Chromium trioxide (1·3 g.) in acetic anhydride (20 ml.) was added to a solution of 1 : 2-dihydrochrysene-1 : 2-dicarboxylic anhydride (1·0 g.) in the same solvent at 80°, and heated for 15 min. on the steam-bath, whereafter a little insoluble material was filtered off and the solution cooled in ice, to give orange crystals. Recrystallisation from benzene gave orange needles of *chrysene*-1 : 2-*dicarboxylic anhydride*, m. p. 218—219° (Found: C, 80·4; H, 3·35. $C_{20}H_{10}O_3$ requires C, 80·5; H, 3·35%), ν 1816, 1756, 1274, 1227, 1193, 1160, 933, 828, 806, 785, 755, 745, and 726 cm.$^{-1}$.

This anhydride (1·0 g.) was treated with aqueous sodium hydroxide (4 g. in 120 ml. of water) at room temperature for 48 hr. The pale buff insoluble matter was removed by filtration and washed with water. Addition of the washings to the filtrate caused precipitation of a white solid, which on filtration, dissolution in water, and acidification by hydrochloric acid gave a pale yellow precipitate, recrystallising from acetic acid as orange needles, m. p. 218—219°. A mixed m. p. with the starting anhydride gave no depression.

We thank Dr. J. Idris Jones for his interest and encouragement, and Mr. W. Kynaston for measurement of the infrared spectra. The work described formed part of the research programme of the Chemical Research Laboratory and is published by permission of the Director.

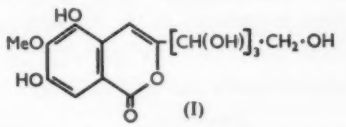
Organic Group, Chemical Research Laboratory, D.S.I.R.,
Teddington, Middlesex. [*Received, January* 21*st*, 1958.]

453. *Bergenin, a C-Glycopyranosyl Derivative of 4-O-Methylgallic Acid.*

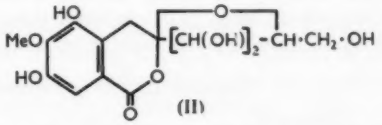
By J. Evelyn Hay and L. J. Haynes.

Bergenin is shown to be the lactone (IV) of 2-β-D-glucopyranosyl-4-*O*-methylgallic acid by studies of light absorption, periodate oxidation, and synthesis.

Bergenin is a colourless crystalline polyphenol which has been isolated from the roots of *Bergenia crassifolia*,[1,2] the bark of *Corylopsis spicata*,[3] and the heartwood of *Shorea leprosula*.[4] There is also evidence [4] that vakerin [5] isolated from the roots of *Caesalpinia digyna* is identical with bergenin. Bergenin was given structure (I) by Tschitschibabin *et al.*[2] in 1928; this was amended to structure (II) by Shimokôriyama [6] in 1950.

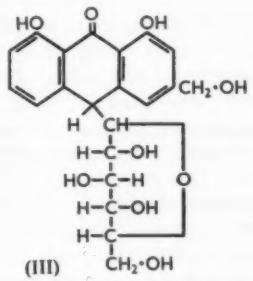


(I)

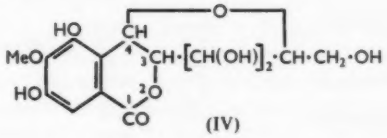


(II)

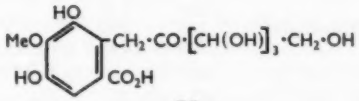
The recent formulation [7] of barbaloin as the *C*-glucopyranosyl compound (III) has led us to search for the presence of this unusual type of sugar linkage in other natural products, and we now present evidence which shows that bergenin should be reformulated as the *C*-glucopyranosyl compound (IV).



(III)



(IV)



(V)

Tschitschibabin *et al.*[2] gave the molecular formula $C_{14}H_{16}O_9,H_2O$ for hydrated bergenin and showed that it contained a lactone ring, one methoxyl group, and two free phenolic hydroxyl groups, but no free carboxyl group. Treatment of bergenin with diazomethane gave a di-*O*-methylbergenin which on permanganate oxidation gave 5 : 6 : 7-trimethoxy-*iso*coumarin-3-carboxylic acid (synthesised by Haworth *et al.*[8] in 1954), 5 : 6 : 7-trimethoxy-*iso*coumarin, and 3 : 4 : 5-trimethoxyphthalic acid. Alkali fusion of bergenin gave 4-*O*-methylgallic acid. Tschitschibabin also reported the formation of a penta-acetyl derivative of bergenin which still contained one active hydrogen atom (Zerewitinoff determination) but could not be further acetylated to yield a hexa-acetate. From these results bergenin was formulated as the *iso*coumarin derivative (I) although no evidence was advanced in support of the linear polyhydroxylic side-chain. Structure (I) does not

[1] Sadikov and Guthner, *Biochem. Z.*, 1927, **190**, 340.
[2] Tschitschibabin, Kirssanow, Korolew, and Woroschzow, *Annalen*, 1929, **469**, 93.
[3] Hattori, *Acta Phytochim., Japan*, 1929, **4**, 327.
[4] Carruthers, Hay, and Haynes, *Chem. and Ind.*, 1957, 76.
[5] Chaudry, Sharma, and Dhar, *J. Sci. Ind. Res., India*, 1954, **13***B*, 147.
[6] Shimokôriyama, *Science, Japan*, 1950, **20**, 576.
[7] Hay and Haynes, *J.*, 1956, 3141; Mühlemann, *Pharm. Acta Helv.*, 1952, **27**, 17.
[8] Haworth, Pindred, and Jefferies, *J.*, 1954, 3617.

explain the resistance to full acetylation and was criticised by Shimokôriyama [6] who proposed the pentahydroxylic structure (II). The evidence for this appears to be based entirely on the fact that bergenin readily reduces Fehling's solution. Shimokôriyama showed that the reducing power of bergenin is comparable with that of glucose, which he explained by formation of a keto-hexose side-chain in ring-opened bergenin (V). It is to be expected from this that di-*O*-methylbergenin would still possess appreciable reducing power. This is not so, and therefore the reducing properties of bergenin itself must be due solely to the presence of the two free phenolic groups and not to a potential reducing group in the side-chain. Moreover, ring-opened di-*O*-methylbergenin does not form a derivative with phenylhydrazine. Since di-*O*-methylbergenin shows no reducing properties, neither structure (I) nor (II) can be correct, since structure (I) should also give the keto-hexose (V) on opening of the lactone ring.

The molecular formula $C_{14}H_{16}O_9,H_2O$ proposed by Tschitschibabin has been confirmed by analysis and by an *X*-ray molecular-weight determination which gave the value 344 ± 4 (required, 346). The carbonyl stretching frequencies in the infrared spectra of bergenin and a number of its derivatives are given in Table 1. It is noteworthy that the

TABLE 1. *Carbonyl stretching frequency of bergenin and its derivatives.*

Compound	ν (cm.$^{-1}$)	Compound	ν (cm.$^{-1}$)
Bergenin hydrate	1699	Tri-*O*-methylbergenin	1737
Anhydrous bergenin	1712, 1682	Penta-*O*-methylbergenin	1740
Di-*O*-methylbergenin	1712	Penta-*O*-acetylbergenin	1780, 1745

TABLE 2. *Ultraviolet-light absorption of bergenin, its derivatives, and related compounds* ($\lambda_{max.}$ *in* mμ).

Compound	$\lambda_{max.}$	log ε	Compound	$\lambda_{max.}$	log ε
Bergenin	275	3·92	*iso*Coumarin	318	3·58
	220	4·42		261	3·87
Di-*O*-methylbergenin	270	3·85		253	3·86
	220	4·42		239	4·22
Penta-*O*-acetylbergenin	254	4·01		228	4·47
	210	4·46	5 : 6 : 7-Trimethoxy*iso*coumarin-3-carboxylic acid	334	3·78
Gallic acid	270	3·89		298	3·96
	210	4·63		288	3·98
Methyl 4-*O*-methylgallate	275	3·99		252	4·52
	218	4·45	5 : 6 : 7-Trimethoxy*iso*coumarin-3-aldehyde	338	3·91
				~270	4·12
				247	4·58

position of the lactonic carbonyl stretching frequency in bergenin and its dimethyl ether is lower than would be expected for a δ-lactone, while those for penta-*O*-acetyl- and tri- and penta-*O*-methyl-bergenin are in the usual region of *ca.* 1740 cm.$^{-1}$. Nevertheless, the carbonyl frequency at 1712 cm.$^{-1}$ in the spectra of anhydrous bergenin and its dimethyl ether are in good agreement with the value of 1716 cm.$^{-1}$ quoted by Blair and Newbold [9] for the carbonyl stretching frequency of the lactonic carbonyl group in mellein (3 : 4-dihydro-3-methyl*iso*coumarin), the spectra of both bergenin and mellein being determined on Nujol mulls. The carbonyl stretching frequency in hydrated bergenin appears at 1699 cm.$^{-1}$ and suggests the presence of a free carboxylic acid group; however, bergenin has no acidic properties, and it has been demonstrated chromatographically that the ring-opened form of bergenin is distinct from bergenin itself and only appears after alkaline treatment of bergenin (followed by acidification). Presumably the water of hydration must be associated with the lactone carbonyl group in order to account for this low carbonyl frequency.

The ultraviolet absorption spectra of bergenin and its methyl ethers (see Table 2) are very similar to that of gallic acid and identical with that of methyl 4-*O*-methylgallate, but they bear little resemblance to the spectrum of *iso*coumarin, the broad band at *ca.*

[9] Blair and Newbold, *J.*, 1955, 2871.

320 mμ characteristic of *iso*coumarin and its derivatives being absent. The carboxylic acid and aldehyde derived from di-*O*-methylbergenin by oxidation possess this characteristic *iso*coumarin spectrum, but the absorbing nucleus of bergenin itself must be that of a dihydro*iso*coumarin in which the conjugated system resembles gallic acid. The disappearance of the broad band at *ca.* 320 mμ in the spectra of the dihydro*iso*coumarins is paralleled in the coumarin series, the spectrum of coumarin having a broad band at 330 mμ which is absent in that of dihydrocoumarin.[10]

The position of the methoxyl group in bergenin relative to the two phenolic hydroxyl groups was established by Tschitschibabin who isolated 4-*O*-methylgallic acid on alkali fusion of bergenin: we have confirmed this by the chromatographic identification of 4-*O*-methylgallic acid with one of the products of hydrolysis of bergenin by barium hydroxide, by the identity of the ultraviolet-light absorption of bergenin and methyl 4-*O*-methylgallate, and by the absence of shift in the ultraviolet absorption of bergenin in presence of aluminium chloride.[11]

The substituted dihydro*iso*coumarin nucleus in bergenin accounts for $C_{10}H_8O_5$ of the total $C_{14}H_{16}O_9$ leaving a side-chain (or chains) containing $C_4H_8O_4$ which must be attached to the nucleus by a carbon–carbon linkage through position 3 in order to account for the formation of the trimethoxy*iso*coumarin-3-carboxylic acid on oxidation. Some difficulty was encountered in determining the number of hydroxyl groups present in this side-chain. The original objection to Tschitschibabin's structure for bergenin arose from the formation of a penta-acetate which still contained one active hydrogen atom. We have repeated the preparation of this penta-acetate and found it to contain five acetyl groups and one active hydrogen (Zerewitinoff determination). An *X*-ray molecular weight determination gave the value 530 (required 538). Analysis of the methyl ethers of bergenin however clearly indicated the presence of only five free hydroxyl groups in bergenin, di-, tri-, and penta-*O*-methylbergenin having respectively three methoxyl groups and three active hydrogen atoms, four methoxyl groups and two active hydrogen atoms, and six methoxyl groups and no active hydrogen. The absence of free hydroxyl groups in penta-*O*-methylbergenin was confirmed by an examination of the infrared spectrum. In the spectrum of the penta-acetate the presence of peaks in the region 3000—3600 cm.$^{-1}$ was barely detectable unless an extremely thick Nujol mull was used. In view of the methylation results and of the periodate oxidation studies to be discussed below, it must be concluded that bergenin contains only five free hydroxyl groups and that the active-hydrogen determinations on the penta-acetate are anomalous. It may be noted that a Zerewitinoff determination on glucose penta-acetate has been reported by Lieff, Wright, and Hibbert [12] to give 1·9 and 1·6 active hydrogen atoms in determinations made with dioxan and pyridine solutions respectively.

Since bergenin contains only five hydroxyl groups there remains one oxygen atom to be accounted for, and this can only be present as an ether oxygen in the side-chain. Di-*O*-methylbergenin rapidly consumes one mol. of periodate, indicating the presence of only two adjacent hydroxyl groups in the side-chain. When di-*O*-methylbergenin is dissolved in alkali, which opens the lactone ring, and the solution is acidified, it can be shown by paper chromatography that re-formation of the lactone ring is slow and that the hydroxy-acid is stable in dilute acid for about 24 hours. Periodate oxidation of such a ring-opened di-*O*-methylbergenin solution results in a rapid consumption of two mols. of periodate, showing that the two free hydroxyl groups in the side-chain must be adjacent to the hydroxyl group involved in lactone ring formation. A solution of periodate-oxidised di-*O*-methylbergenin began to deposit crystals after several days. Their ultraviolet spectrum (Table 2) indicated the presence of an *iso*coumarin nucleus, and they reduced Fehling's solution and formed a semicarbazone and 2 : 4-dinitrophenylhydrazone and contained an aldehyde

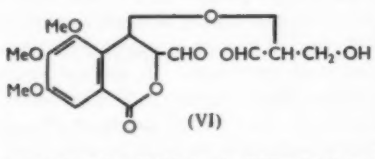
[10] Goodwin and Pollock, *Arch. Biochem. Biophys.*, 1954, **49**, 1.
[11] Swain, *Chem. and Ind.*, 1954, 1480.
[12] Lieff, Wright, and Hibbert, *J. Amer. Chem. Soc.*, 1939, **61**, 865.

XUM

group; this group was in conjugation with the *iso*coumarin nucleus since the ultraviolet spectrum showed a bathochromic shift of 20 mμ compared with that of *iso*coumarin and the maxima in the ultraviolet spectra of the derivatives, at 275 mμ for the semicarbazone and 383 mμ for the 2 : 4-dinitrophenylhydrazone, were characteristic of the derivatives of αβ-unsaturated aldehydes. The infrared spectrum of the aldehyde had peaks at 1754 and 1691 cm.$^{-1}$ attributable to the lactonic and the αβ-unsaturated aldehydic carbonyl group respectively. Analyses of the aldehyde and its semicarbazone agreed with the molecular formula $C_{13}H_{12}O_6$, which accommodates the trimethoxy*iso*coumarin nucleus with a substituent aldehydic group. Since the compound is derived from the oxidative breakdown of the side-chain of di-*O*-methylbergenin the aldehydic group must be linked at position 3 of the nucleus and the compound must be 5 : 6 : 7-trimethoxy*iso*coumarin-3-aldehyde.

Reduction of periodate-oxidised di-*O*-methylbergenin with potassium borohydride followed by acidification [13] afforded glycerol, which was detected chromatographically. Periodate oxidation of di-*O*-methylbergenin therefore gives two fragments, the aromatic nucleus with a side-chain of one carbon atom and a chain of three carbon atoms detected ultimately as glycerol, thus accounting for the four carbon atoms in the side-chain of bergenin, which must be linear, and establishing the position of the ether linkage on the third carbon atom of the side-chain. These observations can only be accommodated by structure (IV) for bergenin since structure (II) has been eliminated.

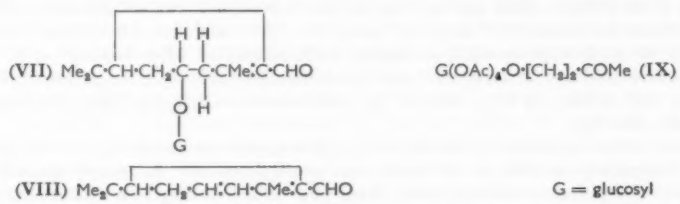
In common with barbaloin (III), bergenin contains the unusual structural feature of a sugar residue attached to the aromatic nucleus by a direct carbon–carbon linkage. Periodate-oxidised barbaloin yields no glycerol on acid treatment of the borohydride reduction product [7] and similar acid-stability of the dialcohol formed by reduction of periodate-oxidised di-*O*-methylbergenin was expected. However it was found that the latter on reduction and treatment with acid yielded glycerol in an amount comparable with that obtained by similar treatment of an *O*-glycosidic compound. The conditions required for cleavage of the ether linkage in periodate-oxidised di-*O*-methylbergenin were therefore studied. Oxidation of di-*O*-methylbergenin by one mol. of periodate must give the dialdehyde (VI) which breaks down slowly at room temperature in the periodate oxidation mixture to give 5 : 6 : 7-trimethoxy*iso*coumarin-3-aldehyde. In the first instance the aldehyde was isolated in low yield from an aqueous solution of di-*O*-methylbergenin which had been oxidised in presence of excess of periodate and set aside for several days before any solid separated. In a controlled oxidation involving equimolar amounts of di-*O*-methylbergenin and sodium metaperiodate, no solid had separated at the end of 16 hours and the ultraviolet absorption of the solution showed maxima characteristic of di-*O*-methylbergenin [the dialdehyde (VI) would however have a similar spectrum]. The solution was neutralised with dilute sodium hydroxide solution, whereupon a flocculent precipitate separated; the solid was isolated and identified by ultraviolet absorption and mixed melting point as the trimethoxy*iso*coumarinaldehyde. The aldehyde also separated from the periodate oxidation mixture on neutralisation with the anion-exchange resin IR-4B(OH$^-$) and its presence was detected spectrophotometrically by the shift in the ultraviolet absorption of the periodate oxidation mixture after addition of a trace of pyridine, a new maximum at 338 mμ characteristic of the trimethoxy*iso*-coumarinaldehyde appearing in the pyridine-treated solution. It appears therefore that the formation of the trimethoxy*iso*coumarinaldehyde from the dialdehyde (VI) is a base-catalysed reaction analogous to the alkaline hydrolysis of glycosides of alcohols substituted in the β-position by a negative group. Ballou [14] has discussed this group of alkali-sensitive



(VI)

[13] Viscontini, Hoch, and Karrer, *Helv. Chim. Acta*, 1955, **38**, 642.
[14] Ballou, *Adv. Carbohydrate Chem.*, 1954, **9**, 88.

glycosides of which the first known was picrocrocin (VII). Kuhn and Löw [15] observed that picrocrocin breaks down in very dilute alkaline solution to D-glucose and the unsaturated aglucone, safranal (VIII), in one stage for which Isbell [16] has proposed a carbanion mechanism in which the unshared electron pair resulting from extraction of a proton by the base co-ordinates with the adjacent carbon atom with formation of a double bond and simultaneous expulsion of the D-glucosyloxy-anion. The D-glucosides of simpler β-hydroxycarbonyl compounds behave similarly, 3′-oxo-*n*-butyl-β-D-glucopyranoside tetra-acetate (IX) breaking down in dilute alkali to D-glucose and methyl vinyl ketone. Moreover, it has been observed [17,18] that separation of the carbon atom bearing the glycosidic linkage by two or more methylene groups from the negative group results in an alkali-stable glucoside. In support of the proposed mechanism for the breakdown of the dialdehyde (VI) we have found that removal of the carbonyl group by reduction to the dialcohol in buffered borohydride solution [19] resulted in an alkali-stable product which did not yield glycerol on further treatment with alkaline borohydride and acid.



Since cleavage of the ether linkage occurs immediately in alkaline solution it was evident that the isolation of glycerol after borohydride reduction of periodate-oxidised di-*O*-methylbergenin was due, not to acid cleavage of the reductionproduct, but to cleavage of the dialdehyde in the strongly alkaline solution produced on addition of borohydride with subsequent reduction of the glyceraldehyde thus produced. This was substantiated by effecting ether-cleavage in a solution of periodate-oxidised di-*O*-methylbergenin (mole/mole) with dilute sodium hydroxide solution, removal of the trimethoxy*iso*coumarin-aldehyde by extraction into chloroform, and chromatographic detection of glycerol in the aqueous residue after treatment with borohydride.

The structure deduced for bergenin has been finally proved by synthesis. We had no information as to the configuration of the side-chain, but model experiments on the condensation of tetra-*O*-acetyl-α-D-glucopyranosyl bromide with methyl 4-*O*-methylgallate in presence of sodium methoxide, designed to give a compound with a structure similar to that proposed for bergenin, in fact gave bergenin. It seems reasonable to assume that the condensation follows the normal pattern for the formation of glycosides and gives a β-D-glucopyranosyl derivative, and that bergenin is hence the lactone of 2-β-D-glucopyranosyl-4-*O*-methylgallic acid.

Experimental

Bergenin (cf. Tschitschibabin *et al.*[2]).—The roots and rhizomes of *Bergenia crassifolia* (1 kg. wet weight) were thoroughly dried in a vacuum-oven at 60° and ground to powder (446 g.) which was poured into acetone (1 l.) contained in a glass column (24 × 2·5 in.). After 16 hr. the column was eluted with acetone (total volume, 2·5 l.), and three fractions were removed. Paper chromatography of each fraction in butanol–acetic acid–water (4 : 1 : 5) and butanol–ethanol–water (4 : 1 : 5) showed the same phenolic component to be present in each fraction, detected

[15] Kuhn and Löw, *Ber.*, 1941, **74**, 219.
[16] Isbell, *Ann. Rev. Biochem.*, 1943, **12**, 214.
[17] Helferich, Richter, and Flechsig, *Ber.*, 1941, **74**, 1019.
[18] Helferich and Schnorr, *Annalen*, 1941, **547**, 201.
[19] Frush and Isbell, *J. Amer. Chem. Soc.*, 1956, **78**, 2844.

XUM

as an orange spot on spraying of the air-dried paper with diazotised sulphanilic acid in 10% aqueous sodium carbonate; no other phenolic products were detected. The fractions were concentrated to brown syrups, dissolved in acetone, and set aside. Crystalline bergenin separated from each fraction, in a total yield of 15 g. Recrystallisation from water yielded the hydrate, m. p. *ca.* 133°. Several recrystallisations from methanol followed by thorough drying (6 hr. at 150°) gave anhydrous bergenin, m. p. 238° [lit., m. p. 130° (hydrate) and 234° (anhyd.)], $[\alpha]_D^{18}$ −37·7° (*c* 1·96 EtOH) (lit., $[\alpha]_D$ −37·3°).

Di-O-methylbergenin (cf. Tschitschibabin *et al.*[2]).—Bergenin (500 mg.) in methanolic solution (10 ml.) was treated with ethereal diazomethane prepared from toluene-*p*-sulphonylmethylnitrosamide.[20] The product (430 mg., 80%) recrystallised from water as a hydrate, m. p. *ca.* 80°; the anhydrous material, m. p. 196° (lit., m. p. 194—196°), was obtained by drying the hydrate over phosphoric anhydride.

Tri- and Penta-O-methylbergenin.—Di-*O*-methylbergenin (3·1 g.) and methyl iodide (50 ml.) were refluxed in dry acetone (85 ml.) until the dimethyl ether had almost completely dissolved. Silver oxide (7 g.) was added in small portions during 3 hr.; dissolution of the dimethyl ether was complete after addition of 2 g. of silver oxide and refluxing for 1 hr. The mixture was refluxed for 1 hr. further, then cooled, the supernatant liquid was decanted and filtered, and the silver residue extracted with hot, dry acetone. The combined filtrate and extracts were concentrated to an orange syrup from which solid separated after storage at 0° overnight. Recrystallisation of the solid from methanol gave needles (300 mg.), m. p. 240—242° [Found: C, 55·3; H, 6·0; OMe, 31·6%; active H, 2·09 atoms. $C_{14}H_{13}O_6(OMe)_3$ requires C, 55·1; H, 5·95; OMe, 33·5%].

The filtrate, after separation of *tri-O-methylbergenin*, was concentrated to a red syrup (3·2 g.) which was completely soluble in methanol and methyl iodide. It was dissolved in methyl iodide (50 ml.) and portions of silver oxide (5 g.) were added during 2 hr. with refluxing. After 3 hr. the mixture was cooled, and the orange solution decanted, filtered, and concentrated together with acetone extracts of the silver residues. The orange syrupy residue (3 g.) partially crystallised on treatment with aqueous methanol, giving *penta-O-methylbergenin* (600 mg.) which recrystallised from water in needles, m. p. 106° after drying over phosphoric anhydride [Found: C, 57·4; H, 7·0; OMe, 45·3%; active H, 0. $C_{14}H_{11}O_4(OMe)_5$ requires C, 57·3; H, 6·6; OMe, 46·3%].

Penta-O-acetylbergenin (cf. Tschitschibabin *et al.*[2]).—Bergenin (100 mg.) was treated with acetic anhydride in dry pyridine solution. The acetate (170 mg.) recrystallised from ethanol as needles, m. p. 207—207·5° (lit., m. p. 199—203°) [Found: C, 53·9; H, 4·7; OAc, 38·0%; active H, 1·01, 1·12; *M*, 530. Calc. for $C_{14}H_{11}O_4(OAc)_5$: C, 53·5; H, 4·9; OAc, 39·9%; *M*, 538].

Periodate Oxidation of Di-O-methylbergenin.—An aqueous solution of di-*O*-methylbergenin (250·9 mg.) and 0·2M-sodium metaperiodate (20 ml.) were mixed, the volume was made up to 100 ml. with distilled water, and the solution set aside at room temperature. A second oxidation mixture containing 277 mg. of di-*O*-methylbergenin was kept at 0°. Within 10 hr. the solution at room temperature had consumed 1·2 mols. of periodate and that at 0° 0·91 mol. of periodate; the periodate uptake was estimated by titration of aliquot parts. The oxidation continued slowly until 2·37 and 2·13 mols. of periodate respectively had been consumed at the end of 5 days.

After 2 days needle-shaped crystals began to separate from the periodate-oxidation mixture, all titrated aliquot portions were retained, and the solids which had separated (60 mg.) were filtered off, washed, dried, and recrystallised by addition of light petroleum (b. p. 60—80°) to a chloroform solution of the solid; it then had m. p. 158—160°.

Periodate Oxidation of Ring-opened Di-O-methylbergenin.—Di-*O*-methylbergenin (136·3 mg.) was dissolved in 0·1N-sodium hydroxide (20 ml.). After 0·5 hr. the pH was adjusted to 5·5 by addition of dilute hydrochloric acid (pH meter). The electrodes were thoroughly rinsed with distilled water, 0·2M-sodium metaperiodate (20 ml.) was added, and the solution made up to 100 ml. A rapid uptake of 2·3 mols. of periodate occurred within 0·5 hr., followed by a slow oxidation rising to 3·4 mols. of periodate consumed during 4 days.

5 : 6 : 7-Trimethoxyisocoumarin-3-aldehyde.—An aqueous solution (60 ml.) of di-*O*-methylbergenin (500 mg., 0·0014 mole) and sodium metaperiodate (600 mg., 0·0028 mole) was left at room temperature overnight. The acid solution (pH 3·24) was neutralised by dilute sodium

[20] De Boer and Backer, *Rec. Trav. chim.*, 1954, **73**, 229.

hydroxide solution, care being taken to avoid the presence of excess of alkali. The flocculent precipitate, which separated immediately on addition of alkali, was extracted into chloroform. The combined extracts were shaken with dilute aqueous sodium thiosulphate, washed with water, and dried. Removal of the solvent gave a pale yellow *aldehyde* (200 mg., 54%) which, recrystallised from chloroform–light petroleum (b. p. 60—80°), had m. p. 158—160° (Found: C, 59·4; H, 4·6. $C_{12}H_{12}O_6$ requires C, 59·1; H, 4·55%). Its *semicarbazone* formed prisms (from methanol), m. p. 233° (Found: C, 51·8; H, 5·1; N, 13·1. $C_{14}H_{15}O_6N_3$ requires C, 52·3; H, 4·7; N, 13·1%), $\lambda_{max.}$ 360, 275 mμ (log ε 4·26, 4·46).

Oxidation of Di-O-methylbergenin by Periodate (1 *Mol.*).—An aqueous solution (5 ml.) of di-*O*-methylbergenin (20 mg., 59 mmoles) and sodium metaperiodate (9 mg., 42 mmoles) was left overnight at room temperature. No trimethoxy*iso*coumarinaldehyde was removed by chloroform even after addition of dilute hydrochloric acid. The solution was divided into 3 portions: (*a*) Dilute sodium hydroxide solution was added to neutrality, and a flocculent precipitate separated which was identified as 5 : 6 : 7-trimethoxy*iso*coumarin-3-aldehyde by its ultraviolet absorption ($\lambda_{max.}$ 247, 338 mμ) and by m. p. and mixed m. p. 158—160°. (*b*) Amberlite resin IR-4B(OH^-) was added to neutralise the solution; after 0·5 hr. needle-shaped crystals separated which were identified as the aldehyde. (*c*) One drop of pyridine was added to the solution and the maximum ultraviolet absorption changed from 270 to 338 mμ.

Reduction of Periodate-oxidised Di-O-methylbergenin by Potassium Borohydride (cf. Viscontini, Hoch, and Karrer [13]).—Sodium metaperiodate (2 mg., 10 mmoles) was added to a solution of di-*O*-methylbergenin (2 mg., 5·9 mmoles) in water (0·2 ml.), and the whole was kept at room temperature for 4 hr. Potassium borohydride (2 mg.) in water (0·1 ml.) was added and the solution kept overnight at room temperature. The solution was heated with N-hydrochloric acid (0·2 ml.) for 15 min. at 100° and placed on a paper chromatogram, with spots of ethylene glycol and glycerol as markers, and allowed to run in ethyl acetate–pyridine–water (10 : 4 : 3). The air-dried paper was sprayed with a mixture of sodium metaperiodate (2%; 4 parts) and alkaline potassium permanganate solution (1% permanganate in 2% aqueous sodium carbonate; 1 part).[21] Glycerol (R_P 0·42) and ethylene glycol (R_P 0·51) yielded yellow spots on a pink ground which developed fully 15 min. after spraying. Di-*O*-methylbergenin gave a yellow spot (R_P 0·42) comparable in intensity with that from sucrose (R_P 0·42) which had been treated in a similar manner.

Reduction of Periodate-oxidised Di-O-methylbergenin by Potassium Borohydride in Buffered Solution.[19]—Di-*O*-methylbergenin (2 mg.) was oxidised as described above. Amberlite resin IR-120(H^+) was added, followed by potassium borohydride (2 mg.) dissolved in 0·05M-boric acid (0·2 ml.). The acid solution was set aside for 24 hr., made strongly alkaline with aqueous sodium hydroxide, and set aside for a further 24 hr. The solution was then acidified with dilute hydrochloric acid, heated for 15 min. at 100°, and placed on a paper chromatogram. No glycerol was detected by the chromatographic method described above.

Reduction of the Periodate Oxidation Mixture after Alkali Cleavage and Removal of 5 : 6 : 7-*Trimethoxyisocoumarin-3-aldehyde.*—The aldehyde was removed by chloroform extraction of a solution of periodate-oxidised di-*O*-methylbergenin which had been neutralised with dilute aqueous sodium hydroxide, and potassium borohydride was added to the aqueous residue. After 16 hr. the solution was acidified with dilute hydrochloric acid, heated at 100° for 15 min., and placed on a paper chromatogram. Glycerol was detected by the method described above.

Hydrolysis of Bergenin by Barium Hydroxide.—Bergenin (20 mg.) in saturated barium hydroxide solution (3 ml.) was heated at 100° for 2 hr. in a sealed tube. The orange solution was acidified by passing it through a column of Amberlite resin IR-120(H^+), and concentrated *in vacuo* to a yellow syrup which was placed on a paper chromatogram and allowed to run in butanol–acetic acid–water (4 : 1 : 5) and butanol–ethanol–water (4 : 1 : 5). Spraying the air-dried papers with a solution of diazotised sulphanilic acid in aqueous sodium carbonate revealed three phenolic components, of R_P 0·56 (yellow), 0·65 (orange), and 0·75 (red), in the neutral solvent; none of these components was identical with bergenin (R_P 0·48). The spots of R_P 0·56 and 0·65 were shown to be acidic by spraying a second paper with an aqueous solution of potassium iodate, potassium iodide, and starch (equal proportions of 0·5% iodate solution and 1% iodide solution containing 0·4% of starch), the acidic components of the mixture giving blue spots on a white ground. The faster-moving acid component ran at the same rate in the

[21] Lemieux and Baur, *Analyt. Chem.*, 1954, **26**, 920.

XUM

two solvent systems, and gave the same colour reaction with diazotised sulphanilic acid, as 4-*O*-methylgallic acid (prepared by hydrolysis of methyl 4-*O*-methylgallate [22]).

Ring-opening of Bergenin and Di-O-methylbergenin.—Bergenin and di-*O*-methylbergenin were dissolved in dilute sodium hydroxide solution, and the solutions acidified with dilute hydrochloric acid and placed immediately on a paper chromatogram along with bergenin and di-*O*-methylbergenin as markers. The mixture was allowed to run in ethyl acetate–acetic acid–water (3 : 1 : 3), the paper was dried in air, and the free acids were detected by spraying with a solution of potassium iodide, potassium iodate, and starch, followed by overspraying with an alkaline solution of diazotised sulphanilic acid. Bergenin had R_F 0·59, the dimethyl ether R_F 0·76, and the free acids R_F 0·46 and 0·65 respectively. The free acid represented *ca.* 90% of the mixture immediately after acidification and ring closure occurred slowly at room temperature, *ca.* 40% of free acid remaining after 24 hr.; however after the solutions had been heated at 100° for 0·5 hr. only a trace of the free acids was detected chromatographically.

Synthetic Bergenin.—The course of the reaction was followed chromatographically, the solvent system being ethyl acetate–acetic acid–formic acid–water (18 : 3 : 1 : 4) and the spray reagent an alkaline solution of diazotised sulphanilic acid.

Sodium methoxide in methanol (4·8 g. of sodium in 150 ml.) was added to a methanolic solution (200 ml.) of tetra-*O*-acetyl-α-D-glucopyranosyl bromide (20 g.) and methyl 4-*O*-methylgallate (10 g.) (prepared by Schöpf and Winterhalder's method [22]). The red solution was left *in vacuo* overnight, diluted with water (200 ml.), and made weakly acid by addition of 2N-acetic acid (85 ml.) Methanol was removed from the clear orange solution by distillation *in vacuo* and the aqueous residue extracted with ether. Methyl 4-*O*-methylgallate (6·5 g.) was recovered from this extract after drying and removal of solvent. The aqueous residue was shown chromatographically to be free from methyl 4-*O*-methylgallate, but contained three phenolic components (R_F 0·43, 0·50, and 0·60). The component of R_F 0·43 was unaffected by hot mineral acid, travelled at the same rate, and gave the same colour reaction with the spray reagent, as bergenin. The components of R_F 0·50 and 0·60 were separated by development on 3 MM paper and elution of the appropriate bands with boiling ethyl acetate. Both components were sensitive to hot mineral acid, the former (R_F 0·50) yielding glucose, methyl 4-*O*-methylgallate, and 4-*O*-methylgallic acid and the latter (R_F 0·60) giving bergenin; hence the first must be the *O*-glycoside of methyl 4-*O*-methylgallate and the second product the methyl ester of the hydroxy-acid formed on ring-opening of bergenin.

Accordingly the aqueous residue from ether-extraction was made strongly acid with 5N-hydrochloric acid and heated for 2 hr. on the water-bath to destroy the acid-labile products. The yellow solution was cooled, and extracted with ether to remove methyl 4-*O*-methylgallate and 4-*O*-methylgallic acid formed on hydrolysis of the *O*-glycoside, and the residue extracted repeatedly with ethyl acetate. The combined extracts were dried and the solvent was removed leaving an orange syrup (1·3 g.) which was dissolved in a small volume of hot water and set aside. Bergenin separated as the hydrate (250 mg.), m. p. and mixed m. p. with the natural product, 130—133°. Several recrystallisations from ethyl acetate followed by thorough drying gave anhydrous bergenin, m. p. and mixed m. p. 230°, $[\alpha]_D^{18}$ −39·3° (*c* 1·908 in MeOH) (lit.,[4] $[\alpha]_D$ −38·5° in MeOH). This gave a penta-acetate, needles (from ethanol), m. p. and mixed m. p. 208°. The infrared spectra of synthetic and natural bergenin and of the penta-acetyl derivatives were identical.

We thank Professor E. L. Hirst, F.R.S., for advice and encouragement, Dr. C. A. Beevers and Dr. H. W. Ehrlich for *X*-ray molecular-weight determinations, Dr. D. M. W. Anderson for infrared spectra, and the Curator of the Royal Botanic Garden, Edinburgh, for supplies of *B. crassifolia*.

DEPARTMENT OF CHEMISTRY,
THE UNIVERSITY, EDINBURGH, 9.
[Present address (L. J. H.): CHEMISTRY DEPARTMENT, UNIVERSITY COLLEGE OF THE WEST INDIES, MONA, ST. ANDREW, JAMAICA.]
[*Received, January 22nd*, 1958.]

[22] Schöpf and Winterhalder, *Annalen*, 1940, **544**, 62.

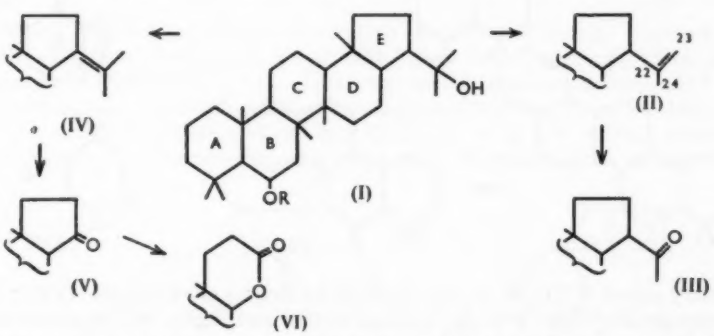
XUM

454. *Triterpenoids. Part XXIV.* Further Investigations on the Constitution of Zeorin.*

By D. H. R. Barton, P. de Mayo, and J. C. Orr.

Stepwise degradation of zeorin has established that this substance contains a group HO·CMe_2– attached to a *cyclo*pentane ring. This has been confirmed, and the relevant ring shown to be terminal, by a reversed Michael reaction whereby five of the six carbon atoms constituting this ring have been isolated as methyl *iso*propyl ketone. The manner in which zeorin, zeorinin, and *neo*zeorinin are related has been clarified and, by a study of further transformation products, a partial structure (XXXV) for the zeorin molecule has been deduced. These and other results, together with a consideration of the place of zeorin in the general triterpenoid biogenetic pattern, have led to the proposal of a squalenoid structural formula (I; R = H) for zeorin.

When the present work began, knowledge concerning the structure of zeorin could be summarised as follows. Zeorin was a secondary-tertiary diol, $C_{30}H_{52}O_2$, of the triterpenoid series [1,2] the former function being contained in a six-membered ring.[3] The tertiary alcoholic group was incorporated in the partial structure, HO·CMe$\langle$C, since dehydration of zeorin acetate led to *iso*zeorinin acetate which contained the grouping $>C{=}CH_2$.[3] That



zeorin was not a derivative of a known pentacyclic triterpenoid was demonstrated by conversion of zeorinin into deoxyzeorinin, in which the tertiary hydroxyl group has been replaced by hydrogen,[2] and thence into the saturated zeorinane,[3] a new triterpenoid hydrocarbon.

The work summarised in the present paper, coupled with biogenetic considerations, leads us to advance (I; R = H) as the constitution of zeorin. This is consistent with prior knowledge and with the following facts.

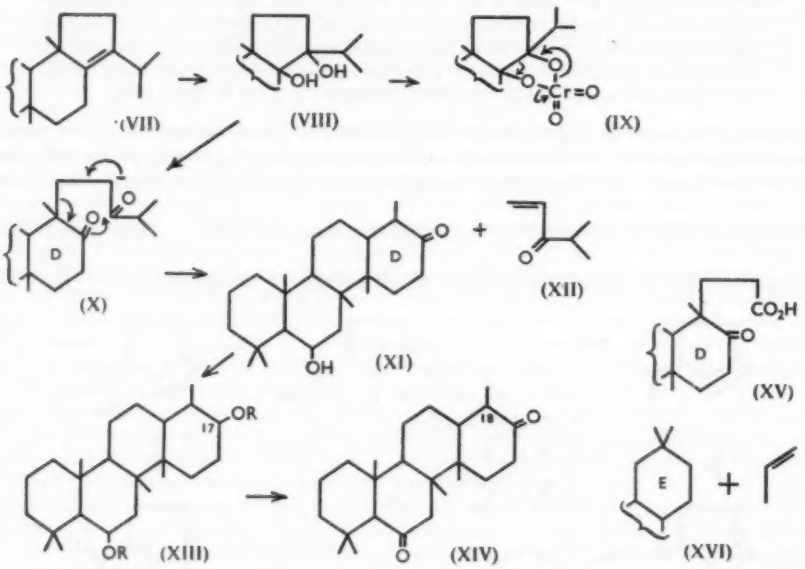
Ozonolysis of crude *iso*zeorinin acetate [3] gave the expected methyl ketone (III; R = Ac) with loss of one carbon atom. This substance had at least four replaceable α-hydrogen atoms (as shown by bromine titration [4]). The crude acetate also afforded acetone on ozonolysis, showing that, if *iso*zeorinin acetate is represented as (II; R = Ac), the *iso*propylidene isomer (IV; R = Ac) must also have been present. Although the latter compound was not obtained pure its presence was confirmed by ozonolysis and further

* Part XXIII, *J.*, 1956, 4160.

[1] Asahina and Akagi, *Ber.*, 1938, **71**, 980.
[2] Asahina and Yosioka, *Ber.*, 1940, **73**, 742.
[3] Barton and Bruun, *J.*, 1952, 1683.
[4] Barnes, Barton, Cole, Fawcett, and Thomas, *J.*, 1953, 571.

oxidation with trifluoroperoxyacetic acid.[5] From this it was possible to isolate a δ-lactone acetate (VI; R = Ac), showing infrared bands in CCl_4 at 1735 and 1248 (acetate) and at 1750 (δ-lactone) cm.$^{-1}$, which must have been derived from the *cyclo*pentanone (V; R = Ac).

Mild acid-catalysed rearrangement of *iso*zeorinin acetate (II; R = Ac) affords[3] zeorinin acetate, which can also be obtained directly from zeorin acetate (I; R = Ac) under the same conditions. On the basis of structure (I; R = H), zeorinin can be represented as (VII; R = H), the following reactions being in agreement with this formulation. Treatment of zeorinin acetate (VII; R = Ac) with osmium tetroxide gave

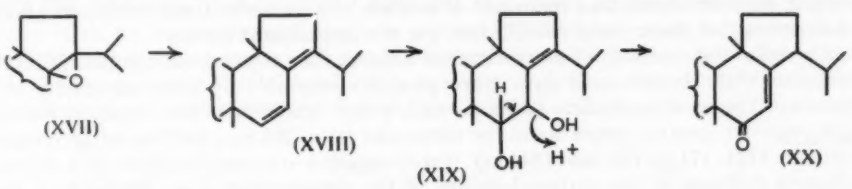


the ditertiary glycol (VIII; R = Ac), which on hydrolysis gives the triol (VIII; R = H). The acetoxy-glycol (VIII; R = Ac) resisted further acetylation with pyridine and acetic anhydride, but was cleaved smoothly by lead tetra-acetate or by chromium trioxide [see (IX; R = Ac)] to the diketone (X; R = Ac). The latter is a 1 : 5-diketone and it was, therefore, predicted that a reverse Michael reaction[6] [see arrows in (X; R = Ac)] would furnish, with loss of six carbon atoms, the hydroxy-ketone (XI) and *iso*propyl vinyl ketone (XII). In the event, base-induced cleavage with potassium hydroxide in diphenyl ether gave methyl *iso*propyl ketone. The loss of one carbon atom (presumably as formaldehyde) from the ketone (XII) has an exact analogy in euphol chemistry.[7] These conditions were unsatisfactory for the isolation of the main fragment of the molecule, but substitution of ethylene glycol for diphenyl ether gave, as non-volatile product, two diols (XIII; R = H), stereoisomeric at $C_{(17)}$. These compounds were isolated as their diacetates (XIII; R = Ac): oxidation of either diol by chromic acid afforded the same diketone (XIV), which had a single infrared band at 1703 cm.$^{-1}$, showing that ring D was six-membered. Reduction of the diketone (XIV) with sodium and propan-2-ol, followed by acetylation, afforded only one of the two diacetates (XIII; R = Ac), obviously that isomer in which both acetate residues are equatorial. The diketone (XIV) was stable to acid, and the

[5] Sager and Duckworth, *J. Amer. Chem. Soc.*, 1955, **77**, 188.
[6] See, for example, Julia, Eschenmoser, Heusser, and Tarköy, *Helv. Chim. Acta*, 1953, **36**, 1885.
[7] Arigoni, Viterbo, Dünnenberger, Jeger, and Ruzicka, *ibid.*, 1954, **37**, 2306.

18-methyl group must therefore, almost certainly, be equatorial. The isolation of the diols (XIII; R = H), rather than the hydroxy-ketone (XI), is an example of the familiar base-catalysed oxidation-reduction system [8] formed by alcohols (in this case ethylene glycol) and ketones [in this case (XI)]. This sequence of reactions proves the attachment of the HO·CMe_2– group of zeorin to a *terminal* five-membered ring.

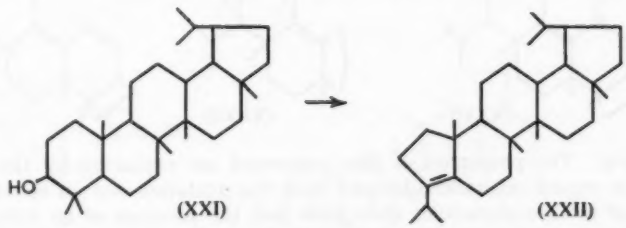
Whilst these and other investigations were being pursued an account of some experiments by Ryabinin and Matyukhina appeared.[9] These authors by direct chromic acid oxidation of zeorin obtained a C_{27} diketo-acid. This substance, which we now formulate as (XV), enabled the Russian workers to deduce the presence, in zeorin, of a HO·CMe_2– group attached to a *cyclo*pentane ring, though the assumption that it was necessarily terminal is unwarranted. These authors, however, formulate zeorinin as a ring-expansion



(XVII) (XVIII) (XIX) (XX)

product [as (XVI)], a view in no way compatible with our results. It is interesting that we have found that ozonolysis of zeorinin acetate at −60° leads to the known epoxide,[2] whilst Ryabinin and Matyukhina obtained, by ozonolysis at room temperature, a " stable ozonide."

It was next desirable to effect entrance into the D-ring of zeorin. Zeorinin epoxide (XVII; R = H), by acid-catalysed dehydration,[2] gives dehydrozeorinin, which must now be represented as (XVIII; R = H). Treatment of dehydrozeorinin benzoate [3] (XVIII; R = Bz) with osmium tetroxide, followed by cleavage of the osmate with lithium aluminium hydride, afforded a mixture of the triol (XIX; R = H) and of its 3-monobenzoate (XIX; R = Bz). A corresponding reaction with dehydrozeorinin acetate (XVIII;



(XXI) (XXII)

R = Ac) and isolation of the osmate by the hydrogen sulphide method gave the unsaturated ketone (XX; R = Ac). This must have been formed, possibly by traces of mineral acid entrained in the hydrogen sulphide gas stream, through the allylic carbonium ion [see (XIX; R = Ac)]. Compound (XX; R = Ac) showed a *cyclo*hexenone infrared band at 1660 $cm.^{-1}$ and had an ultraviolet absorption band at 230 mμ. The formulation of dehydrozeorinin as (XVIII; R = H) is, of course, supported by Asahina and Yosioka's observation [2] that, on hydrogenation, it re-forms zeorinin (VII; R = H).

In order to provide a model for the reactions of zeorinin (VII; R = H), lupanol [10] (XXI) was dehydrated with phosphorus pentachloride and the mixture of hydrocarbons obtained was isomerised with ethanolic hydrochloric acid as in the standard method [1] for converting zeorin into zeorinin. A homogeneous hydrocarbon, the previously known

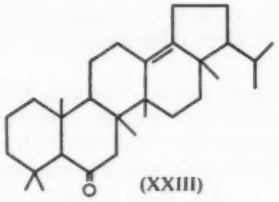
[8] For example, Doering and Aschner, *J. Amer. Chem. Soc.*, 1949, **71**, 839; and references there cited.
[9] Ryabinin and Matyukhina, *Zhur. obshchei Khim.*, 1957, **27**, 277.
[10] Ames, Halsall, and Jones, *J.*, 1951, 450.

XUM

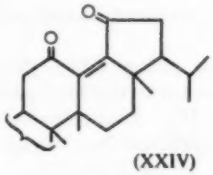
iso-γ-lupene [11] (XXII), resulted. The reactivity of this hydrocarbon towards peracetic acid and ozone was the same as that of zeorinin and its derivatives, the known oxide [11] (as XVII) being formed. On treatment with acid as in the preparation of dehydrozeorinin the oxide gave dehydro-*iso*-γ-lupene [(as (XVIII)], whose optical properties were comparable with those of dehydrozeorinin.

In our earlier paper on zeorin,[3] it was reported that under strongly acidic conditions zeorininone afforded a highly crystalline isomer, *neo*zeorininone. If zeorininone is to be based on structure (VII; R = H), then there is available excellent analogy in the conversion of quinovic acid into novic acid [12] and in other comparable rearrangements [13,14] to suggest that *neo*zeorininone should be represented as (XXIII). The preparation of this ketone has been improved by using perchloric acid in acetic acid for the rearrangement, whilst it has been shown that treatment of zeorinin acetate under these conditions affords a non-conjugated diene whose constitution was not investigated further.

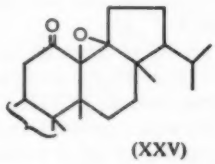
The following reactions of *neo*zeorininone support the proposed constitution (XXIII). Oxidation with chromic acid gave three products separable by chromatography over alumina. The most instructive of these was a yellow triketone of the empirical formula $C_{30}H_{44}O_3$. Its spectral properties in the ultraviolet ($\lambda_{max.}$ 263 mμ) and the infrared region (bands at 1724, 1717, 1707, and 1644 cm.$^{-1}$) corresponded to a *cisoid* enedione and, further, indicated that one of the carbonyl groups of the chromophore was situated in a five-



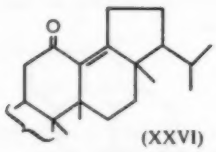
(XXIII)



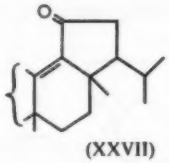
(XXIV)



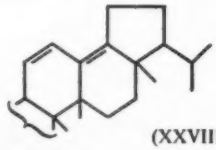
(XXV)



(XXVI)



(XXVII)



(XXVIII)

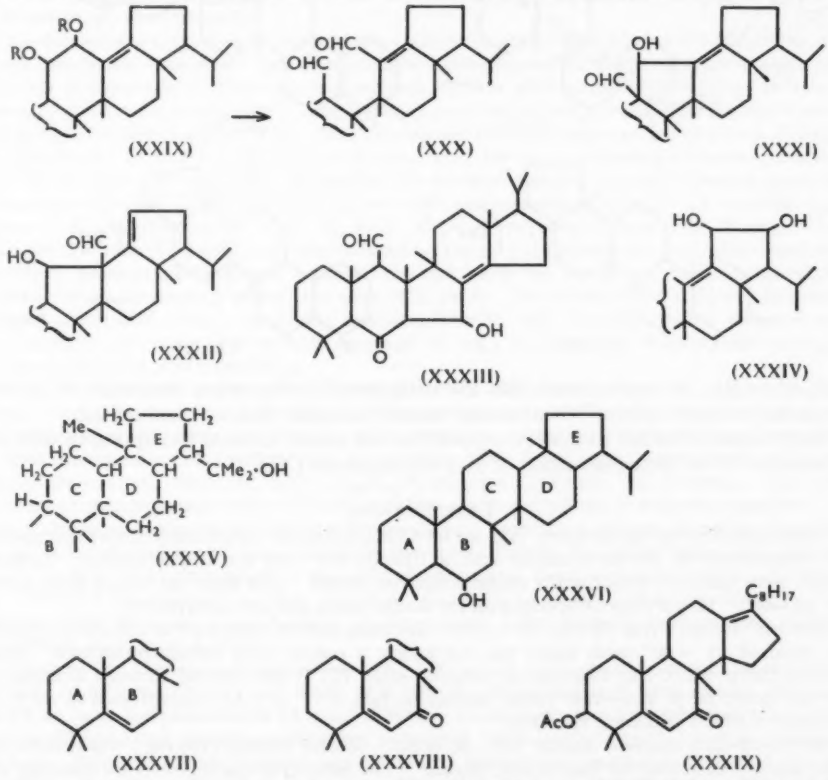
membered ring. The properties of this compound are explained by the constitution (XXIV). The second substance obtained from the oxidation was an epoxide for which the absence of intense ultraviolet absorption and the presence of an infrared band at 1703 cm.$^{-1}$ (characteristic of a *cyclo*hexanone) indicated structure (XXV). In agreement, reduction of this epoxide by chromous chloride gave, in excellent yield, the related conjugated ketone (XXVI) having an ultraviolet maximum at 255 mμ and infrared bands at 1700, 1670, and 1603 cm.$^{-1}$. Significantly the band at 1603 cm.$^{-1}$, to be attributed to the double bond, had the high intensity associated with *cisoid* αβ-unsaturated ketones. Finally, the third product from the oxidation was an αβ-unsaturated ketone whose composition and spectral properties require that it be represented as (XXVII).

Oxidation of *neo*zeorininone (XXIII) with selenium dioxide in dioxan at 140° afforded a conjugated heteroannular diene (XXVIII), reconverted into *neo*zeorininone on hydrogenation. The diene (XXVIII) showed intense absorption indicative of a *transoid* chromophore. On treatment with osmium tetroxide it afforded a disecondary diol

[11] Nowak, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1949, **32**, 323.
[12] Barton and de Mayo, *J.*, 1953, 3111.
[13] Allan, Spring, Stevenson, and Strachan, *J.*, 1955, 3371.
[14] Allan, Fayez, Spring, and Stevenson, *J.*, 1956, 457, and references there cited.

(XXIX; R = H), readily acetylated to the diacetate (XXIX; R = Ac). Cleavage of the diol (XXIX; R = H) with lead tetra-acetate furnished, *via* the dialdehyde (XXX), an aldol condensation product. This showed no ultraviolet absorption and had infrared bands in CCl_4 at 3553 (hydrogen-bonded hydroxyl), 2720 (aldehyde), 1708 (*cyclo*hexanone), and 1695 (hydrogen-bonded aldehyde) cm.$^{-1}$. The isolated ketone group in *neo*zeorininone (XXIII) absorbed at 1713 cm.$^{-1}$ in the same solvent. This aldol can be represented by structure (XXXI), (XXXII), or (XXXIII). The infrared data and stability to base speak against (XXXIII) and we favour (XXXI). What is important about this aldol is that its formation excludes the formula (XXXIV) for the parent diol.

If the relationship between zeorininone and *neo*zeorininone postulated above is accepted, the facts so far summarised prove that zeorin must have the partial structure (XXXV). Previous investigations[3] indicated that the secondary hydroxyl group of zeorin could not be in a terminal ring. In terms of (XXXV) this means that the secondary hydroxyl group is in ring B. This was confirmed in the following way. Deoxyzeorin (XXXVI) was dehydrated with toluene-*p*-sulphonyl chloride and pyridine[3] to a mixture of olefins, whose main component[3] must be (XXXVII) and, in agreement, chromic acid



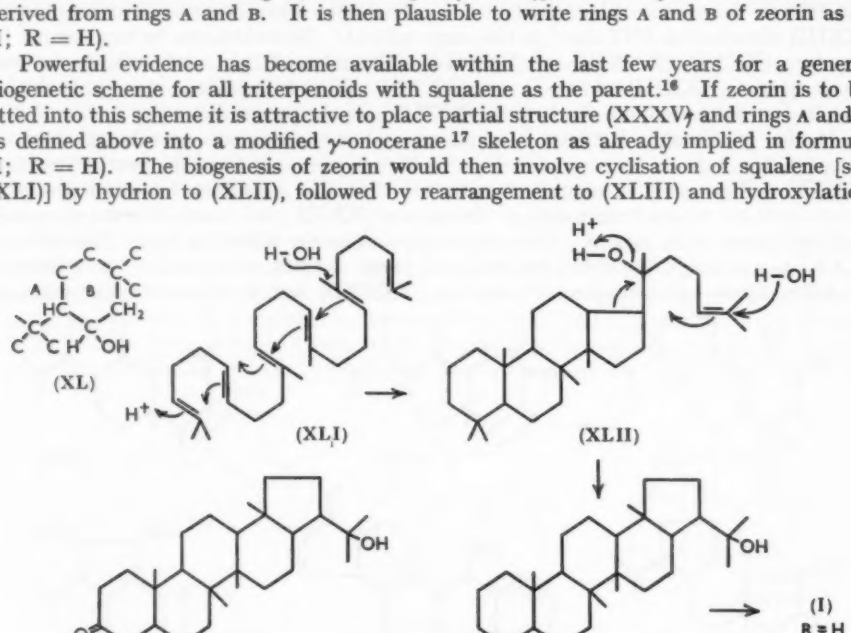
(XXIX) (XXX) (XXXI) (XXXII) (XXXIII) (XXXIV) (XXXV) (XXXVI) (XXXVII) (XXXVIII) (XXXIX)

oxidation of the mixture afforded an αβ-unsaturated ketone (XXXVIII). This had an infrared band at 1650 (*cyclo*hexenone) cm.$^{-1}$ and showed ultraviolet absorption at 239 mμ, very close to that (238 mμ) of a derivative of butyrospermol acetate (XXXIX) described by Lawrie, Hamilton, Spring, and Watson.[15] This ketone was stable to vigorous treatment with bromine or selenium dioxide, in agreement with the lack of replaceable

[15] Lawrie, Hamilton, Spring, and Watson, *J.*, 1956, 3272.

α-hydrogen atoms. These experiments show that ring B of zeorin contains the partial structure (XL). We recall also that Asahina and Yosioka [2] obtained, by dehydrogenation of zeorin, 1 : 2 : 5-trimethylnaphthalene. It seems improbable that this hydrocarbon could come from rings C, D, and E [see (XXXV)], but it may be more reasonably derived from rings A and B. It is then plausible to write rings A and B of zeorin as in (I; R = H).

Powerful evidence has become available within the last few years for a general biogenetic scheme for all triterpenoids with squalene as the parent.[16] If zeorin is to be fitted into this scheme it is attractive to place partial structure (XXXV) and rings A and B as defined above into a modified γ-onocerane [17] skeleton as already implied in formula (I; R = H). The biogenesis of zeorin would then involve cyclisation of squalene [see (XLI)] by hydrion to (XLII), followed by rearrangement to (XLIII) and hydroxylation



to (I; R = H). It is of interest that the triterpenoid hydrocarbon taraxerene [18] has also been isolated from a lichen,[19] for this may arise by a similar hydrion mechanism.

Very recently further biogenetic support for our zeorin formula has appeared with the elucidation [20,21] of the constitution of hydroxyhopanone (XLIV).

Experimental

Unless specified to the contrary, $[\alpha]_D$ are for $CHCl_3$ solutions; ultraviolet absorption spectra were determined on EtOH solutions with a Unicam S.P. 500 spectrophotometer. Infrared spectra were taken on Nujol mulls unless otherwise stated. The light petroleum used was of b. p. 40—60°. M. p.s were determined on the Kofler block and are uncorrected.

Zeorinin Acetate Oxide (XVII; R = Ac).—Zeorinin acetate (300 mg.) in chloroform (5 ml.) was ozonised at −60° until there was no longer a colour with tetranitromethane. After isolation the product was dissolved in benzene–ether (9 : 1) and filtered through alumina, to give the oxide, m. p. 245—251° (from methanol), $[\alpha]_D$ +77° (*c* 0·44), undepressed in m. p. on admixture with an authentic specimen.[3]

22-Oxo-23-norisozeorinin Acetate (III; R = Ac).—Zeorin acetate (700 mg.) was dehydrated in the manner described by Barton and Bruun.[3] The total hydrocarbon mixture resulting was ozonised in chloroform at −60° until no further colour was given with tetranitromethane.

[16] Ruzicka, *Experientia*, 1953, **9**, 357.
[17] Barton and Overton, *J.*, 1955, 2639.
[18] Beaton, Spring, Stevenson, and Stewart, *J.*, 1955, 2131; Brooks, *J.*, 1955, 1675; and references there cited.
[19] Bruun, *Acta Chem. Scand.*, 1954, **8**, 1291.
[20] Dunstan, Fazakerley, Halsall, and Jones, *Croat Chem. Acta*, in the press.
[21] Schaffner, Caglioti, Arigoni, Jeger, Fazakerley, Halsall, and Jones, *Proc. Chem. Soc.*, 1957, 353.

Isolation of the product, chromatography, and elution with benzene–light petroleum (7 : 3), gave the *acetate* (III; R = Ac) (250 mg.), m. p. 232—238° (decomp.) (from methanol), $[\alpha]_D$ +44° (*c* 0·93) (Found: C, 78·9; H, 10·55. $C_{31}H_{50}O_3$ requires C, 79·1; H, 10·7%). This gave, in the usual way, a 2 : 4-*dinitrophenylhydrazone*, m. p. 239—240° (Found: N, 8·6. $C_{37}H_{54}O_6N_4$ requires N, 8·6%). The ketone gave a positive Zimmerman test and on titration (38·6 mg.) with bromine in acetic acid (10 ml.) took up 4·4 mol.; under the same conditions pregnenolone (45·3 mg.) took up 4·1 mol.

Isolation of the Lactone Acetate (VI; R = Ac). Zeorin acetate (3 g.) was dehydrated and ozonised as described in the preceding experiment. The product, in benzene solution, was filtered through alumina to give an oil (1·75 g.). This was dissolved in methylene dichloride (30 ml.) containing anhydrous sodium phosphate (1·5 g.) and trifluoroperoxyacetic acid (1 g.), and the mixture refluxed for 15 min. Isolation and alkaline hydrolysis gave an acid fraction which after acetylation (acetic anhydride–pyridine) was chromatographed over alumina. Elution with methanol–acetic acid (9 : 1) and crystallisation from aqueous methanol gave the *lactone acetate* (VI; R = Ac), m. p. 282—285° (decomp.), $[\alpha]_D$ +43° (*c* 1·0) (Found: C, 75·75; H, 10·5. $C_{29}H_{46}O_4$ requires C, 75·95; H, 10·1%). In a similar experiment the ozonolysis product from dehydrated zeorin acetate (500 mg.) was steam-distilled and the distillate treated with 2 : 4-dinitrophenylhydrazine. Acetone 2 : 4-dinitrophenylhydrazone, identified by m. p. and mixed m. p., was obtained.

Dehydration and Oxidation of Deoxyzeorin.—Zeorin acetate (4·17 g.) was dehydrated in the manner previously described [3] and the product hydrogenated in acetic acid over platinum. The crude deoxyzeorin acetate was treated with lithium aluminium hydride (3 g.) in ether–dioxan, to give crude deoxyzeorin. The latter, in pyridine (40 ml.), was refluxed with toluene-*p*-sulphonyl chloride (6 g.) for 8 hr. The crystallised hydrocarbon mixture obtained (1·74 g.) (see Barton and Bruun [3]) was refluxed in acetic acid (80 ml.) containing chromium trioxide (2 g.) for 20 min. Filtration of the product in benzene solution through alumina gave the αβ-unsaturated *ketone* (XXXVIII), m. p. 186—187° (from methanol), $[\alpha]_D$ −51° (*c* 1·51), $\lambda_{max.}$ 239 mμ (ε 12,100) (Found: C, 85·2; H, 11·5. $C_{30}H_{48}O$ requires C, 84·85; H, 11·4%). The unsaturated ketone (21·2 mg.) in a 0·0025N-solution (25 ml.) of bromine in acetic acid containing a catalytic amount of hydrogen bromide was set aside for 36 hr. at room temperature. Isolation then gave starting material in over 80% yield. The ketone (15·5 mg.) was heated in refluxing acetic acid (3 ml.) containing selenium dioxide (100 mg.) for 16 hr.: isolation and crystallisation then gave the starting material (6 mg.) identified in this and the previous experiment by m. p. and mixed m. p.

Reaction of Zeorinin Acetate with Osmium Tetroxide.—Zeorinin acetate (817 mg.) in dioxan (7 ml.) containing osmium tetroxide (643 mg.) was set aside in the dark for 14 days. Decomposition of the osmic ester with hydrogen sulphide and working up in the usual way gave the *triol monoacetate* (VIII; R = Ac), m. p. 248—254° (from light petroleum), $[\alpha]_D$ +53° (*c* 2·37) (Found: C, 76·7; H, 10·7. $C_{32}H_{54}O_4$ requires C, 76·45; H, 10·85%). This was recovered unchanged after treatment with pyridine–acetic anhydride at room temperature.

The above monoacetate (50 mg.) in dioxan (4 ml.) containing lithium aluminium hydride (50 mg.) was refluxed for 30 min. Isolation and crystallisation from light petroleum gave the *triol*, m. p. 255—270°, unchanged on repeated crystallisation from methanol or light petroleum, $[\alpha]_D$ +31° (*c* 2·40) (Found: C, 78·1; H, 11·5. $C_{30}H_{52}O_3$ requires C, 78·0; H, 11·4%). The triol was also obtained by reduction of the osmate ester formed with zeorinin acetate with lithium aluminium hydride.

3-*Acetoxy*-17 : 21-*dioxo*-A-seco*zeorinane* (X; R = Ac).—(*a*) Zeorinanetriol monoacetate (343 mg.) in benzene (25 ml.) and acetic acid (20 ml.) containing lead tetra-acetate (500 mg.) was left at room temperature for 10 min. Previous experimentation had indicated that under these conditions 1 mol. of tetra-acetate was consumed, there being no further uptake on longer standing. Ethylene glycol (5 drops) was added and the product isolated in the usual way, to give the *acetoxy-dione* (X; R = Ac), m. p. 125—128° (from methanol), $[\alpha]_D$ +32° (*c* 3·33) (Found: C, 76·7; H, 10·6. $C_{32}H_{52}O_4$ requires C, 76·75; H, 10·45%).

(*b*) The triol monoacetate (30 mg.) in acetic acid (25 ml.) containing chromium trioxide (9·3 mg.) was kept at room temperature for 80 min., after which isolation afforded the dione. A similar result was achieved by using the chromium trioxide–pyridine complex as the oxidant.

The Reversed Michael Reaction.—(*a*) The dione monoacetate (X; R = Ac) (118 mg.) was added to a refluxing mixture of diphenyl ether and potassium hydroxide whilst a stream of

XUM

nitrogen was passed through it and into an aqueous solution of 2 : 4-dinitrophenylhydrazine in dilute sulphuric acid. A precipitate was immediately formed and continued to accumulate for 45 min. Collection, followed by chromatography on bentonite–kieselguhr to remove the diphenyl ether–2 : 4-dinitrophenylhydrazine adduct, afforded methyl *iso*propyl ketone 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 121—122° (Found: C, 50·15; H, 5·35; N, 20·9. Calc. for $C_{11}H_{14}O_4N_4$: C, 49·6; H, 5·3; N, 21·0%). In a similar experiment the volatile ketone from 127 mg. of the dione was passed into an aqueous solution of semicarbazide acetate. Methyl *iso*propyl ketone semicarbazone, m. p. and mixed m. p. 112—113°, was obtained.

(*b*) Diethylene glycol (15 ml.) containing potassium hydroxide (0·5 g.) was refluxed and a stream of nitrogen passed through the mixture. The dione (742 mg.) was dropped into the solution and heating continued for 40 min. The product was filtered through alumina; the material (413 mg.) eluted with more powerful eluants than benzene–carbon tetrachloride (1 : 6) was acetylated (acetic anhydride–pyridine), and the product was rechromatographed. Elution with carbon tetrachloride–benzene (3 : 1) then gave the *diacetate-I* (XIII; R = Ac), m. p. 194—195° (from methanol), $[\alpha]_D$ +83° (*c* 1·24) (Found: C, 75·25; H, 10·25. $C_{28}H_{46}O_4$ requires C, 75·3; H, 10·4%). Elution with benzene gave the *diacetate-II* (XIII; R = Ac), m. p. 213—215° (from methanol or light petroleum), $[\alpha]_D$ +41° (*c* 1·16) (Found: C, 75·55; H, 10·45%).

The diacetate-II (25 mg.) in dioxan (1 ml.) was treated with a solution of lithium aluminium hydride (40 mg.) in ether (1 ml.), and the ether distilled off. The mixture was then refluxed for 15 min. The product (23 mg.) in pyridine (2 ml.) containing chromium trioxide (30 mg.) was kept overnight at room temperature. Crystallisation from methanol gave the *diketone* (XIV), m. p. 212—216°, $[\alpha]_D$ +15° (*c* 0·35) (Found: C, 80·35; H, 10·75. $C_{24}H_{38}O_2$ requires C, 80·4; H, 10·7%). The same diketone (m. p. and mixed m. p.) was obtained from the diacetate-I. The diketone was unchanged after 30 min. in refluxing chloroform containing concentrated hydrochloric acid.

The diketone (10 mg.) in dry benzene (3 ml.) and propan-2-ol (2·5 ml.) was refluxed during the addition of sodium (1 g.) in small pieces during 4 hr. Acetylation (acetic anhydride–pyridine) of the product gave the diacetate-II (8 mg.), identified by m. p., mixed m. p., and rotation.

Dehydrozeorinin (XVIII; R = H) *and its Derivatives.*—Dehydrozeorinin benzoate (268 mg.) in dioxan (15 ml.) containing lithium aluminium hydride (300 mg.) was refluxed for 5 min. Crystallisation from methanol gave dehydrozeorinin (XVIII; R = H), m. p. 174—183°, $[\alpha]_D$ +79° (*c* 1·71) (Found: C, 84·8; H, 11·25. Calc. for $C_{30}H_{48}O$: C, 84·85; H, 11·4%). Acetylation (pyridine–acetic anhydride) gave the acetate (XVIII; R = Ac), m. p. 222—223°, $[\alpha]_D$ +75° (*c* 1·89).

Reaction of Dehydrozeorinin Derivatives with Osmium Tetroxide.—(*a*) Dehydrozeorinin benzoate (187 mg.) in dioxan (8 ml.) containing osmium tetroxide (95 mg.) was set aside in the dark for 5 days. Addition of lithium aluminium hydride (200 mg.) in ether (3 ml.) followed by filtration of the product in carbon tetrachloride through alumina and elution with benzene–carbon tetrachloride (1 : 19) gave the *triol monobenzoate* (XIX; R = Bz), m. p. 227—241° (from methanol or light petroleum), $[\alpha]_D$ +55° (*c* 0·57) (Found: C, 78·8; H, 10·1. $C_{37}H_{54}O_4$ requires C, 78·95; H, 9·65%). Elution of the column with benzene then gave the corresponding *triol* (XIX; R = H), m. p. 235—252° (from methanol), $[\alpha]_D$ +35° (Found: C, 78·3; H, 11·4. $C_{30}H_{50}O_3$ requires C, 78·55; H, 11·0%).

(*b*) Dehydrozeorinin acetate (894 mg.) in dioxan (25 ml.) containing osmium tetroxide (485 mg.) was left for 4 days at room temperature in the dark. Hydrogen sulphide from a Kipp generator was then passed in. The product, in carbon tetrachloride solution, was chromatographed over alumina (activity III; 17 g.). Elution with varying proportions of ether in benzene gave the unsaturated *ketone* (XX; R = Ac), m. p. 141—142° (from aqueous methanol), $[\alpha]_D$ +76° (*c* 0·66), $\lambda_{max.}$ 230 mμ (ε 9000) (Found: C, 76·85; H, 10·3. $C_{32}H_{50}O_3,H_2O$ requires C, 76·75; H, 10·45%).

neo*Zeorininone.*—Zeorininone (1·29 g.) in acetic acid (100 ml.) at 100° was treated with 72% perchloric acid (6·5 ml.) and heating continued for 40 min.; this gave *neo*zeorininone (XXIII) (1·05 g.), identified by m. p. and mixed m. p.

Acid Treatment of Zeorinin Acetate.—Zeorinin acetate (805 mg.) in acetic acid (50 ml.) at 100° was treated with 72% perchloric acid (2 ml.). After 4 min. the product had separated as white crystal clusters which recrystallised from ethanol to give a *diene*, m. p. 177—179°, $[\alpha]_D$ +50° (*c* 2·13) (Found: C, 88·15; H, 11·9. $C_{30}H_{48}$ requires C, 88·15; H, 11·85%).

XUM

Selenium Dioxide Oxidation of neo*Zeorininone*.—*neo*Zeorininone (424 mg.) and selenium dioxide (133 mg.) in dioxan (2 ml.) were heated in a sealed tube at 140° for 1 hr. The product was chromatographed over alumina (activity I: 15 g.). Elution with benzene–carbon tetrachloride (1 : 1) gave *dehydroneozeorininone* (XXVIII), m. p. 255—256° (from methanol), $[\alpha]_D$ +30° (*c* 1·34), $\lambda_{max.}$ 265, 255, and 247 mμ (ε 20,600, 29,000, and 26,100 respectively) (Found: C, 85·5; H, 10·75. $C_{30}H_{46}O$ requires C, 85·25; H, 10·95%).

This dienone (31 mg.) in *cyclo*hexane–acetic acid was hydrogenated in the presence of Adams catalyst. Crystallisation of the product gave *neo*zeorininone (m. p. and mixed m. p.). The infrared spectrum was identical with that of an authentic specimen.

Dehydroneozeorininone-11 : 12-diol (XXIX; R = H).—The dienone (110 mg.) in pyridine (1 ml.) containing osmium tetroxide (200 mg.) was kept in the dark for 12 days. Decomposition of the osmate ester with hydrogen sulphide and crystallisation from light petroleum gave a *diol* (XXIX; R = H), m. p. 214—221°, $[\alpha]_D$ +33° (*c* 1·24) (Found: C, 78·8; H, 11·0. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·6%). The m. p. of the product was unchanged by chromatography. *neo*Zeorininone was recovered unchanged after being kept with osmium tetroxide for 6 weeks under similar conditions.

The diol (65 mg.) with acetic anhydride–pyridine gave the *diacetate* (XXIX; R = Ac), m. p. 103—106° (from methanol), $[\alpha]_D$ +12° (*c* 1·41) (Found: C, 75·5; H, 10·0; Ac, 15·4. $C_{32}H_{52}O_5$ requires C, 75·5; H, 9·7; 2Ac, 15·9%).

The diol (23·2 mg.) consumed 1 mol. of lead tetra-acetate in 5 min., no further oxidation taking place. Isolation of the product gave, after crystallisation from light petroleum, an *aldol* (? XXXI), m. p. 173—181°, $[\alpha]_D$ −119° (*c* 1·14) (Found: C, 78·7; H, 10·3. $C_{30}H_{46}O_3$ requires C, 78·9; H, 10·6%). This showed no intense absorption in ethanol or ethanolic potassium hydroxide.

Oxidation of neo*Zeorininone*.—*neo*Zeorininone (1·62 g.) in acetic acid (1 l.) was added to chromium trioxide solution in acetic acid (1·08N; 20 ml.) and the mixture left overnight at room temperature. The product was chromatographed on alumina (activity V; 35 g.) to give the following products:

(i) Elution with carbon tetrachloride gave the *dione* (XXVII), m. p. 278—282° (from ethanol), $[\alpha]_D$ +39° (*c* 1·67), $\lambda_{max.}$ 259 mμ (ε 12,800), $\nu_{max.}$ 1697 cm.$^{-1}$ (merged *cyclo*pentenone and *cyclo*hexanone) (Found: C, 82·30; H, 10·8. $C_{30}H_{46}O_2$ requires C, 82·15; H, 10·55%).

(ii) Elution with benzene–carbon tetrachloride (1 : 1) gave the *epoxy-dione* (XXV), m. p. 272° to >350° (from light petroleum), $[\alpha]_D$ +91° (*c* 1·05), $\lambda_{max.}$ 288 mμ (ε 108) (Found: C, 79·15; H, 10·1. $C_{30}H_{46}O_3$ requires C, 79·25; H, 10·2%). It gave a negative tetranitromethane test. The wide m. p. range was due to conversion into a higher-melting compound at the m. p.

(iii) Elution with benzene–ether (1 : 4) and crystallisation from methanol gave the yellow *trione* (XXIV), m. p. 284—290°, $[\alpha]_D$ +31° (*c* 0·89), $\lambda_{max.}$ 263, 375 mμ (ε 9200 and 460 respectively) (Found: C, 79·6; H, 9·7. $C_{30}H_{44}O_3$ requires C, 79·6; H, 9·8%).

*Reduction of the Epoxy*neo*dione* (XXV).—The epoxide (106 mg.) in acetone (15 ml.) was added to ethanolic chromous chloride [22] (0·63N; 9 ml.). Isolation of the product after 50 min. gave *isoneo*zeorinindione (95 mg.), m. p. 266—268° (from light petroleum), showing a sharp change from needles to prisms at 235—236°, $[\alpha]_D$ +53° (*c* 1·2), $\lambda_{max.}$ 255 mμ (ε 8400) (Found: C, 81·95; H, 10·2. $C_{30}H_{46}O_3$ requires C, 82·15; H, 10·55%).

iso-γ-*Lupene*.—Lupanol (354 mg.) in dry light petroleum (40 ml.) containing phosphorus pentachloride (400 mg.) was left at 0° for 1 hr. Isolation of the product and filtration in light petroleum solution through a short column of alumina gave a crystalline mixture of hydrocarbons. The mixture (200 mg.) in ethanol (300 ml.) containing concentrated hydrochloric acid (50 ml.) was refluxed for 35 min. Crystallisation from methanol gave *iso*-γ-lupene,[11] m. p. 135—136°, $[\alpha]_D$ +13° (*c* 2·88) (Found: C, 87·95; H, 12·15. Calc. for $C_{30}H_{50}$: C, 87·75; H, 12·25%).

iso-γ-*Lupene Epoxide*.—(*a*) *iso*-γ-Lupene (163 mg.) in methylene dichloride (10 ml.) was ozonised at 0° until the solution gave no colour with tetranitromethane. Filtration of the product in light petroleum through alumina (activity III; 8 g.) gave the epoxide,[11] m. p. 179—187° (from acetone), $[\alpha]_D$ +5° (*c* 1·24) (Found: C, 84·4; H, 11·75. Calc. for $C_{30}H_{50}O$: C, 84·45; H, 11·8%).

(*b*) *iso*-γ-Lupene (282 mg.) in acetic acid (50 ml.) at 100° was treated with 30% hydrogen

[22] Cole and Julian, *J. Org. Chem.*, 1954, **19**, 131; Julian, Cole, Meyer, and Regan, *J. Amer. Chem. Soc.*, 1955, **77**, 4601.

peroxide (1 ml.). After 7 min. isolation and crystallisation afforded the same epoxide, identified by m. p. and mixed m. p.

Dehydro-iso-*γ*-*lupene*.—The epoxide (see above) (24 mg.) in ethanol (20 ml.) containing concentrated hydrochloric acid (2 ml.) was refluxed for 90 min., the minimum amount of chloroform (*ca.* 0·5 ml.) being added to prevent the separation of an oil. Filtration of the product in light petroleum through alumina (activity I; 1 g.) gave *dehydro*-iso-*γ*-*lupene*, m. p. 111—112° (from acetone), $[\alpha]_D$ +30°, $\lambda_{max.}$ 252 mμ (ε 21,500) (Found: C, 87·8; H, 11·7. $C_{30}H_{48}$ requires C, 88·15; H, 11·85%).

This work was made possible through the generosity of Professor and Mrs. N. A. Sörensen and Dr. T. Bruun of the Norges Tekniske Høgskole (Trondhjem) who supplied us with zeorin. We express our deep thanks for this gift. We thank the Government Grants Committee of the Royal Society and Imperial Chemical Industries Limited for financial assistance. We also acknowledge the valuable help of Dr. D. A. J. Ives in some of the experiments

THE UNIVERSITY, GLASGOW, W.2.
IMPERIAL COLLEGE, LONDON, S.W.7.

[*Received, January 28th*, 1958.]

---

455. *Electrical Conductances of Solutions in Nitric Acid. Part II.* Solutions of Alkali-metal Nitrates. Transport Numbers and Ionic Conductances of* NH_4^+, K^+, NO_2^+, *and* NO_3^- *Ions.*

By W. H. LEE and D. J. MILLEN.

The electrical conductivities of solutions of ammonium, sodium, and potassium nitrates in nitric acid have been measured. The electrode reactions occurring in such solutions are $NO_2^+ + e \longrightarrow NO_2$ and $NO_3^- \longrightarrow NO_2^+ + \frac{1}{2}O_2 + 2e$; these were used to yield transport numbers and ionic conductances of NH_4^+, Na^+, and K^+ ions in solutions of the nitrates. Transport numbers of NO_2^+ and NO_3^- ions in solutions of dinitrogen pentoxide, and of water, in nitric acid have also been determined. The mobilities of both these ions, produced in the self-dissociation of nitric acid, are normal, showing that in this solvent there is no significant contribution from a chain-conductance mechanism. The conductances of the alkali-metal nitrates are interpreted in connection with the self-dissociation of the solvent.

A technique is described in which conductance measurements are used analytically in transport-number determinations.

NITRIC ACID at −10° is an approximately half-molar solution of nitrate and nitronium ions and water.* Its conductivity shows it to be a good ionising solvent for dinitrogen pentoxide, $NO_2^+NO_3^-$, so it might be expected that alkali-metal nitrates, $M^+NO_3^-$, would form highly conducting solutions in it.

Interpretation of the conductivities of the solutions requires the fraction of the conductivity to be ascribed to each ion present to be determined, so we measured transport numbers for the alkali-metal ions, and for the nitronium and nitrate ions, also present in these solutions. The allocation of transport numbers in turn requires investigation of the reactions which occur upon electrolysis.

All these initially colourless solutions become yellow in the cathode compartment of a Hittorf transport cell. This is not due to thermal decomposition, for the contents of the centre and anode compartments remain colourless; it is the result of the cathode process:

$$NO_2^+ + e \longrightarrow NO_2$$

Although nitrogen dioxide is largely ionised in nitric acid solution,[1] sufficient remains un-ionised to produce a yellow colour. The cathodic formation of stoicheiometric nitrogen dioxide was found to be quantitative for the electrolysis both of the solvent and of the

* Part I, *J.*, 1956, 4463.

[1] Millen and Watson, *J.*, 1957, 1369.

solutions of alkali nitrates: 1 mole of stoicheiometric NO_2 is liberated for the passage of one Faraday.

During electrolysis of the pure acid or of solutions of alkali nitrates, oxygen is evolved at the anode:

$$NO_3^- \longrightarrow NO_3^+ + \tfrac{1}{2}O_2 + 2e$$

Again this process is quantitative: 5·6 l. of oxygen are evolved for the passage of one Faraday.

If the solutions initially contain nitrogen dioxide, an alternative reaction appears to occur preferentially at the anode:

$$NO_2 \longrightarrow NO_3^+ + e$$

Hence, if the anode solution is originally strongly coloured, no oxygen is evolved until the solution has become almost colourless.

Experimental

Materials.—Nitric acid and dinitrogen pentoxide were prepared as described in Part I. Good quality distilled water of specific conductance below 10^{-6} ohm^{-1} at laboratory temperature was used in view of the very high conductance of these solutions. "AnalaR" sodium and potassium nitrates were crushed and dried at 110° for several hours and stored over phosphoric oxide. "AnalaR" ammonium nitrate was not heated, but was kept over phosphoric oxide for some weeks before use.

Verification of Electrode Reactions.—Solutions of dinitrogen pentoxide, and of alkali nitrates, in nitric acid were electrolysed in a Pyrex glass U-tube of about 100 ml. capacity. The anode, of bright platinum gauze, was placed just below the surface of the solution in one arm; this end of the tube was connected *via* a capillary of small dead-space, to a jacketed gas-burette, in which the volume of evolved gas could be measured over saturated brine. The cathode consisted of about 1 cm.[2] of bright platinum foil, and was fitted into the other arm by a ground-glass joint.

The solutions were electrolysed at 25 mA at 0°, the U-tube and burette being surrounded by circulating ice-cold water. The quantity of electricity was measured by a copper coulometer in series; periods of electrolysis were from 6 to 8 hr.

The volume of gas evolved was measured. The gas was transferred to Hempel bulbs and absorbed in 15% alkaline pyrogallol solution; the residual volume of gas never exceeded 10% of the total, and in most cases it was about 5%. After electrolysis all the solution was run out and titrated for stoicheiometric NO_2. Aliquot parts were diluted with water, excess of standard potassium permanganate added, and the excess was determined by addition of potassium iodide and titration with standard thiosulphate solution. At this dilution the nitric acid does not oxidise the iodide. For results see Table 1. The average values are 1·02 moles of nitrogen dioxide and 0·240 mole of oxygen liberated per Faraday.

Table 1. *Investigation of electrode reactions.*

Solute	Molality	O_2 at N.T.P. (l. F^{-1})	NO_2 liberated (mole F^{-1})	Solute	Molality	O_2 at N.T.P. (l. F^{-1})	NO_2 liberated (mole F^{-1})
N_2O_5	0·030	5·28	1·20	$NaNO_3$	0·059	5·09	0·95
,, ...	0·036	5·85	1·06	,, ...	0·088	5·61	1·06
,, ...	0·087	5·55	1·07	,, ...	0·093	5·58	0·86
,, ...	0·091	5·59	1·08	KNO_3	0·084	4·95	0·96
,, ...	0·122	4·99	0·90	,, ...	0·362	5·32	—

Transport-number Determinations.—(a) *Solutions of alkali nitrates in nitric acid.* The solutions were electrolysed between bright platinum electrodes in a modified Hittorf apparatus. The compartments, of about 8 ml. volume, were joined by taps sealed with solution. The anode compartment consisted of a bulb joined by about 20 cm. of capillary tubing to the centre compartment. This long path was essential to ensure that the product of the electrode reaction did not subsequently migrate from this compartment. For the same reason it was necessary

[3] MacInnes, "Principles of Electrochemistry," Reinhold, New York, 1939, p. 33.

XUM

to restrict the period of electrolysis at 25 mA to about 4 hr. The gas evolved at the anode escaped through tubes of phosphoric oxide. The quantity of electricity passed was measured by a copper coulometer in series with the cell, the necessary corrections being applied.[2]

After electrolysis the compartments were isolated, and their contents siphoned into weighed, stoppered bottles, and analysed for the alkali cation. Solutions of sodium and potassium nitrates were evaporated to dryness; the residue was carefully warmed with concentrated sulphuric acid and finally ignited to the alkali sulphate, with the addition of a small amount of ammonium carbonate to assist in the decomposition of bisulphate. Solutions of ammonium nitrate were diluted, and excess of concentrated sodium hydroxide solution was added, followed by Kjeldahl distillation of the ammonia into excess of standard acid.

(b) *Solutions of dinitrogen pentoxide, and of water, in nitric acid.* The overall effect of electrolysis of these solutions is to change the concentration of dinitrogen pentoxide. Since the solvent may itself be regarded as an 85·7% (w/w) solution of this solute in water, chemical analysis would not be sufficiently accurate to record the change produced by the small amount of electrolysis occurring in a normal transport-number determination. The cell, basically of Hittorf type, was therefore so designed that the change in composition could be derived from measurements of electrical conductivity before and after electrolysis by use of subsidiary electrodes in the anode and centre compartments. These compartments also had capillary side-arms for thorough pre-mixing of their contents with a stream of dry nitrogen. Their cell-constants were measured with 0·1D-potassium chloride as usual.

TABLE 2. *Conductivities of solutions of alkali-metal nitrates in nitric acid at* −10·02°.

$NaNO_3$ (m)	$10^4\kappa$ (ohm^{-1})	KNO_3 (m)	$10^4\kappa$ (ohm^{-1})	KNO_3 (m)	$10^4\kappa$ (ohm^{-1})	NH_4NO_3 (m)	$10^4\kappa$ (ohm^{-1})
0·0338	365·7	0·0515	386·0	0·3828	571·9	0·1067	421·5
0·0725	382·6	0·1007	409·2	0·5919	698·8	0·2002	479·0
0·1881	467·9	0·1685	455·3	0·7737	789·8	0·2480	507·3
0·2951	522·1	0·2152	476·7	1·0682	883·8	0·3879	586·6
0·4052	565·8	0·2943	535·9	1·2301	902·9	0·5325	685·3
0·4862	593·8	0·3355	538·0	1·5825	924·6	0·6929	757·2
0·5874	640·6					0·9053	835·5
0·7017	681·9					0·9881	876·5
0·8038	700·8					1·0551	890·1
1·1290	798·8						

TABLE 3. *Densities (d, g. ml.$^{-1}$) of solutions of alkali-metal nitrates in nitric acid at* −10·02°.

$NaNO_3$ (m)	d	KNO_3 (m)	d	NH_4NO_3 (m)	d
0·2786	1·5773	0·2427	1·5794	0·3183	1·5661
0·3580	1·5810	0·4958	1·5937	0·5597	1·5720
0·5210	1·5893	0·7021	1·6075	0·9208	1·5763
0·7019	1·5982	0·7478	1·6078	0·9561	1·5775
0·9459	1·6094	1·0480	1·6249	1·1841	1·5801

TABLE 4. *Transport numbers of the* Na^+, K^+, *and* NH_4^+ *ions in solutions in nitric acid at* −10·02°.

$NaNO_3$ (m)	$t(Na^+)$	KNO_3 (m)	$t(K^+)$	NH_4NO_3 (m)	$t(NH_4^+)$
0·1706	0·132	0·0992	0·106	0·1121	0·094
0·2920	0·186	0·2591	0·191	0·2488	0·190
0·4618	0·233	0·2714	0·218	0·3302	0·215
0·5982	0·247	0·4605	0·273	0·4375	0·253
0·7071	0·263	0·5877	0·297	0·5289	0·258 *
0·859	0·278	0·7575	0·324 *	0·6325	0·276

* One result only; other values are means of the results obtained from analysis of anode and cathode compartments.

The cell was filled with solution, the compartments were isolated, and the initial conductivities determined. The compartments were then joined and a current of 25 mA was passed for about 4 hr. The cells were then isolated, the contents of each was mixed by the

passage of dry nitrogen, and their final electrical conductivities were determined. The conductivity–concentration data from Part I then yielded the changes in composition.

Conductivities of Solutions.—Conductivities were determined as described in Part I, the same type of cell and the same temperature, −10°, being used.

Results.—Solutions of alkali-metal nitrates in nitric acid. The electrode reactions which occur on electrolysis of these solutions are:

$$NO_3^- \longrightarrow NO_2^+ \times \tfrac{1}{2}O_2 + 2e \text{ (anode)}; \quad NO_2^+ + e \longrightarrow NO_2 \text{ (cathode)}$$

There is a net gain of alkali nitrate, MNO_3, in the cathode compartment, and a net loss in the anode compartment in each case of $t(M^+)$ moles per Faraday, where $t(M^+)$ is the transport number of the alkali-metal cation for the solution. No change is expected in the centre compartment.

As these solutions contain two cations, M^+ and NO_2^+, the value of $t(NO_3^-)$ cannot be obtained directly from $t(M^+)$. Again, the graph of $t(M^+)$ against concentration does not extrapolate to a non-zero value for $t^0(M^+)$ as the concentration of alkali nitrate tends to zero since

$$\lim_{m \to 0} t(M^+) = \lim_{m \to 0} [m.u(M^+)/\sum mu] = 0$$

where u is the mobility of the ion of molality m.

Results are in Tables 2, 3, and 4 for sodium potassium, and ammonium nitrates in nitric acid.

The solvent used, prepared and purified as described in Part I, is not quite anhydrous, but as exact corrections for the effect of the small quantity of water cannot be made the tabulated values are those directly observed. Such corrections would lead to slightly higher values for the specific conductances, but would not change the reported ionic conductances significantly.

Solutions of dinitrogen pentoxide in nitric acid. The electrode reactions are the same as for solutions of alkali-metal nitrates. Passage of one Faraday leads to a net gain of $[0{\cdot}5 - t(NO_2^+)]$ moles of dinitrogen pentoxide in the anode compartment. The amount of dinitrogen pentoxide in the anode compartment did increase, showing that $t(NO_2^+) < 0{\cdot}5$; from this increase the transport numbers were evaluated. No change should occur in the centre compartment.

The change in the cathode compartment could not be used, since one mole of nitrogen dioxide is liberated per Faraday passed. This is a strong electrolyte [3] and its presence will offset the decrease in conductivity due to loss of dinitrogen pentoxide. However, in this case it is permissible to put $t(NO_3^-) = 1 - t(NO_2^+)$, since there are only two ionic species present in the solution.

Transport numbers obtained from measurements on the anode compartment are in Table 5.

TABLE 5. *Transport number of the* NO_2^+ *ion in solutions of dinitrogen pentoxide in nitric acid at* −10·02°.

N_2O_5 (initial molality)	0·056	0·082	0·107	0·195	0·211	0·350	0·515
$t(NO_2^+)$	0·363	0·365	0·375	0·385	0·389	0·421	0·436

DISCUSSION

Ionic Conductances.—For a solution of specific conductance κ, of several ions, u_i being the mobility of the ion of molarity m_i, t_i its transport number and l_i its ionic conductance:

$$\kappa = \sum_i \frac{m_i u_i F}{1000} \qquad t_i = \frac{m_i u_i}{\sum_i m_i u_i} \qquad l_i = u_i F = \frac{1000\,\kappa\, t_i}{m_i}$$

Ionic conductances calculated from these equations for the concentration range 0—1M are recorded in Table 6. The transport numbers have been interpolated at intervals of 0·1 molarity from the molal data in Table 4.

[3] Unpublished work.

XUM

The conductance of each ion varies only slowly with increasing concentration. Thus good evidence is provided to support the assumption made in certain calculations in Part I, that ionic conductances can be taken as approximately independent of concentration over the range 0—1M.

The ionic conductances of the nitrate and nitronium ions cannot be similarly calculated since, in the absence of data concerning activity coefficients, the molarities of these ions in solutions of dinitrogen pentoxide in nitric acid are unknown, but the ionic conductances in the special case of the solvent, nitric acid, can be obtained for the molarity is known (Part I). Combining the equivalent conductance of the solvent with the appropriate nitrate and nitronium ion transport numbers, we obtain the ionic conductances. Values of l, compared with those of the alkali-metal cations, are: NO_3^-, 46·6; NO_2^+, 25·1; Na^+, 21·7; K^+, 27·2; NH_4^+, 22·8. The values for nitrate and nitronium ions refer to the solvent. The values for alkali-metal cations were obtained by extrapolation of the data of Table 6 to zero cation concentration.

TABLE 6. *Ionic conductances of* Na^+, K^+, *and* NH_4^+ *ions in solutions of the nitrates in nitric acid at* −10·02°.

Molarity ...	0·1	0·2	0·3	0·4	0·5	0·6	0·7	0·8	0·9	1·0
t	0·057	0·103	0·143	0·175	0·197	0·216	0·232	0·245	0·255	0·263
l } Na^+	21·7	21·8	22·3	21·9	20·9	20·2	19·5	18·8	18·1	17·5
t	0·070	0·127	0·170	0·206	0·234	0·256	0·273	0·285	0·297	0·309
l } K^+	27·2	27·1	26·4	26·0	25·5	24·9	24·3	23·6	23·2	22·9
t	0·058	0·107	0·154	0·189	0·217	0·243	0·267	0·281	0·315	0·340
l } NH_4^+ ...	22·8	23·3	24·4	24·2	23·9	23·9	24·2	24·0	25·6	26·7

The mobility of the nitronium ion is comparable with that of the alkali-metal cations. Although the mobility of the nitrate ion is higher, Table 5 shows that under certain conditions $t(NO_2^+) = 0{\cdot}436$ and $t(NO_3^-) = 0{\cdot}564$. If it is accepted that the conductance of the nitronium ion is normal, then it is unlikely that under these conditions there is a contribution to the conductance of the nitrate ion from a chain mechanism. Although, with decrease of concentration, $t(NO_3^-)$ increases to 0·637, it does not seem probable that within this range a change in conductance mechanism occurs.

Interpretation of Conductances.—The conductance of a solution of an alkali-metal nitrate in nitric acid can be divided into contributions from the added salt and from the ions produced in the self-dissociation of the solvent. The contribution of the latter falls as the alkali-metal nitrate concentration increases, but remains dominant until a concentration of about 0·4M-alkali nitrate is reached. The rate of increase of conductance with concentration for dilute solutions of alkali-metal nitrates is consequently markedly dependent on the self-dissociation equilibrium constant. The contribution of the metal cation to the conductance is known from transport measurements. The remainder of the conductance provides a measure of the concentrations of nitrate and nitronium ions which are related through the self-dissociation equilibrium constant. The dependence is complicated to some extent by the variations of ionic mobilities and activities with changing concentration. Lack of information about both of these factors limits the accuracy with which the extent of the self-dissociation of nitric acid can be evaluated from conductance data on solutions of alkali-metal nitrates.

For a solution of alkali metal nitrate MNO_3, of molarity m and density d, the composition of 1 litre of solution can be expressed as n moles of NO_2^+ and H_2O, $(n + m)$ moles of NO_3^-, m moles of M^+, and $c = (1000d - \sum xM)/63{\cdot}03$ moles of NHO_3, where x is the molarity of species of molecular weight M. The classical equilibrium constant, in terms of molar fractions, is given by:

$$K = \frac{n^2(n+m)}{c^2(c+3n+2m)} = K'X \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where $K' = n^2(n + m)$ and $X = 1/[c^2(c + 3n + 2m)]$

Calculation shows that X varies only slowly with m; over the range $m = 0{\cdot}1$ to $1{\cdot}0$, X varies by only 0·35%. Neglecting this slight dependence of X on m, we have from eqn. (1):

$$dn/dm = -n/(3n + 2m) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

The specific conductance of the solution, in terms of the ionic mobility l for each species present, can be written:

$$1000\,\kappa = n.l(NO_2^+) + (n + m).l(NO_3^-) + m.l(M^+) \quad . \quad . \quad . \quad . \quad (3)$$

If, in this approximate treatment, we may neglect the variation of the ionic mobilities with concentration, we have:

$$1000\,d\kappa/dm = l(NO_2^+).dn/dm + l(NO_3^-).(1 + dn/dm) + l(M^+) \quad . \quad (4)$$

By combining equations (2) and (4) an expression is obtained for the measured quantity $d\kappa/dm$, in terms of the unknown quantity n:

$$1000\,d\kappa/dm = -l(NO_2^+)[n/(3n + 2m)] + l(NO_3^-)[(2n + 2m)/(3n + 2m)] + l(M^+)$$

For the limiting case $m \longrightarrow 0$, $n \longrightarrow a$, the equilibrium concentration of dissociation products in the pure solvent, we can write: $l = 1000\kappa t/a$ for the nitrate and nitronium ions, where t is the appropriate transport number. The expression for a then simplifies to:

$$a = \frac{\kappa[2t(NO_3^-) - t(NO_2^+)]}{3[d\kappa/dm - l(M^+)/1000]}$$

in which all quantities are limiting ones for $m \longrightarrow 0$. Evaluation of a yields, from the data on solutions of sodium, potassium, and ammonium nitrates respectively, the values 0·64, 0·59, and 0·56M. Differences between the values are to be expected, since no account has been taken of the variations with concentration of activity coefficients and ionic mobilities, on neither of which is there any information. The values for a agree reasonably with that evaluated from conductance measurements on solutions of water and dinitrogen pentoxide for which, because of the special relation between the two solutes and the solvent, another method of evaluation was possible.

The award of a Further Education and Training Grant by the Ministry of Education (to W. H. L.) is gratefully acknowledged.

Battersea College of Technology, London, S.W.11.
William Ramsay and Ralph Forster Laboratories,
University College, London, W.C.1.

[*Received, August 2nd,* 1957.]

XUM

456. *The Mechanisms of Inhibition and Retardation in Radical Polymerizations. Part IV.* The Effects of Diphenylpicrylhydrazine and a Condensation Product of Acetone with Phenylhydroxylamine upon the Sensitized Polymerization of Styrene.*

By J. C. Bevington and N. A. Ghanem.

Both diphenylpicrylhydrazine (I) and *N*-(3-*N*-hydroxyanilino-1 : 3-dimethylbutylidene)aniline *N*-oxide (II) retard the radical polymerization of styrene at 60°. By using labelled retarders it has been shown that both substances become chemically incorporated in the polymers; if the concentration of retarder is sufficient, the number of initiator fragments combined in each polymer molecule is approximately 1 and the number of retarder molecules is approximately 0·5. The use of these retarders in the determination of rates of initiation in radical polymerizations is discussed; it is concluded that the *N*-oxide (II) could be used for this.

Apart from the mechanism by which they act, retarders of radical polymerizations are of interest since they might be used for determining rates of initiation in certain polymerizations. Rates of initiation in sensitized polymerizations can be determined by using labelled sensitizers,[1] but this cannot be done for other types of radical polymerization. For example, a reliable method is needed for measuring rates of initiation in graft copolymerizations and in studies of branching reactions, and here labelled retarders might be used.

A retarder which functions by becoming attached to the growing end of a polymer chain and completely deactivating it was sought. The number of monomer units associated with one retarder molecule could be determined by analysis of the polymer and would be the kinetic chain length (ν) in the polymerization; the rate of initiation is then the ratio of the overall rate of polymerisation to ν. Substances which might behave as such retarders include stabilized radicals which can react with other radicals but not with monomer molecules. If the retarder did not combine with the polymer radical, its action might be represented as

$$R\cdot + X\cdot \longrightarrow P + Y \qquad . \; . \; . \; . \; . \; . \; . \; . \; (1)$$

where R· is a growing polymer radical, X· a stabilized radical, P a dead polymer molecule, and Y a stable product derived from X. In this case, it would be necessary to determine the quantity of Y produced instead of the quantity of retarder incorporated in the polymer, but no suitable stabilized radical was discovered.

Another possibility is to use a substance, such as a quinone, which can add to the end of a growing polymer radical to form a new radical so stabilized that it is incapable of further growth. *p*-Benzoquinone behaves thus during the polymerization of methyl methacrylate;[2] the product of the interaction of a polymer radical and a quinone molecule can be represented as (III) where P represents a poly(methyl methacrylate) chain. Almost all these radicals disappear by combination with another polymer radical to give the molecule (IV). In this case, one molecule of combined retarder represents two polymer radicals. With other monomers, different effects occur[3] and so *p*-benzoquinone could not be used generally for measuring rates of initiation.

A substance X·H whose hydrogen atom is easily removed by polymer radicals can be regarded as a transfer agent; if however the radical X· is so stabilized that it cannot re-initiate a polymer chain and can only combine with a second polymer radical, then the

* Part III, Bevington and Ghanem, *J.*, 1956, 3506.

[1] Bevington, *Trans. Faraday Soc.*, 1955, **51**, 1392.
[2] Bevington, Ghanem, and Melville, *Trans. Faraday Soc.*, 1955, **51**, 346.
[3] Bevington, Ghanem, and Melville, *J.*, 1955, 2822.

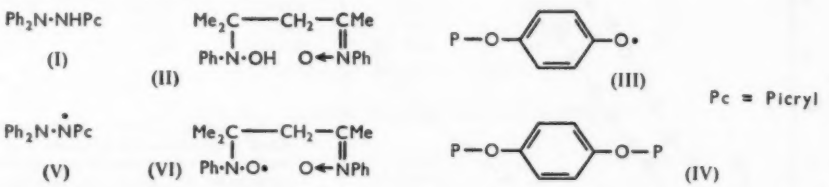
XUM

substance X·H is then a retarder and not a transfer agent. Each molecule, as represented by equations (2) and (3), terminates two growing chains and on the average each polymer

$$P\cdot + X\cdot H \longrightarrow P\cdot H + X\cdot \quad \ldots\ldots\ldots \quad (2)$$

$$P\cdot + X\cdot \longrightarrow P\cdot X \quad \ldots\ldots\ldots \quad (3)$$

molecule contains half a molecule of retarder. If transfer to solvent or monomer occurs each kinetic chain contains on the average half a molecule of retarder, and it is still possible to measure the rate of initiation.



The substances (I) and (II) can quite easily lose hydrogen atoms and so be converted into the radicals diphenylpicrylhydrazyl (V) and (VI) which are stabilized and inhibit radical polymerizations.[4] The substances (I) and (II) are retarders for certain polymerizations, and it seems quite likely that their action might be according to equations (2) and (3).

The objects of the work now described were to discover the mechanism by which substances (I) and (II) retard, and to examine the possibility of using them to measure rates of initiation. The work involved the use of ^{14}C-labelled specimens of (I), (II), and αα′-azo*iso*butyronitrile.

Experimental

Materials and Methods.—The preparations of labelled azo*iso*butyronitrile [5] and labelled diphenylpicrylhydrazine [6] have been described. The labelled specimen of the *N*-oxide (II) was prepared by Banfield and Kenyon's method [7] from [1 : 3-$^{14}C_2$]acetone supplied by the Radiochemical Centre, Amersham. Experimental procedures have been described.[3] Polymerizations were allowed to go to about 6% conversion. In the results, the activities of the various materials are quoted in counts per min. (c./min.) for a fixed weight of carbon dioxide in a gas counter; these counting rates are directly proportional to the $^{14}C : {}^{12}C$ ratios in the materials being assayed. For this method of assay, a counting rate of 14,000 c./min. corresponds to a specific activity of about 1μc/g. of carbon.

Results.—Separation tests. The removal from polymers of all traces of uncombined labelled reagents is very important in tracer studies of polymerizations. If polystyrene is prepared with αα′-azo*iso*butyronitrile as initiator,[5] virtually all traces of uncombined initiator can be removed by precipitating the polymer twice from benzene with methanol. Tests were made concerning the separation of polystyrene from the retarders (I) and (II). Unlabelled polymer was mixed in solution with labelled retarder; the polymer was recovered by precipitation and

Table 1.

	Retarder (I)	Retarder (II)
Polystyrene (mg.)	164·3	625
Retarder (mg.)	11·5	103
Counting rate for retarder (c./min.)	56,200	161,000
Counting rate (c./min.) calc. for no separation	2200	18,400
Counting rate (c./min.) obs. for polymer after 1, 2, and 3 pptns. respectively	3, 1, 0	480, 17, 7

then assayed. The results (Table 1) show that two precipitations suffice to remove almost all traces of the uncombined hydrazine (I) from the polymer, but in the case of the *N*-oxide (II)

[4] Bevington and Ghanem, *J.*, 1956, 3506.
[5] Bevington, Melville, and Taylor, *J. Polymer Sci.*, 1954, **12**, 449.
[6] Bevington, *J.*, 1956, 1127.
[7] Banfield and Kenyon. *J.*, 1926, 1612.

XUM

three precipitations may be necessary; in routine experiments two and three precipitations respectively were used.

Experiments with the hydrazine (I) *as retarder.* Bulk styrene was polymerized at 60° by using a fixed concentration of the azo-compound as initiator and various concentrations of the hydrazine (I). Results of experiments with labelled initiator or retarder are summarized in Tables 2 and 3 and Fig. 1. For the unretarded polymerization the rate of polymerization is steady; when retarder is present, the rate gradually rises during the reaction. N_i and N_r are the numbers of molecules of initiator fragments or retarder molecules per polymer molecule.

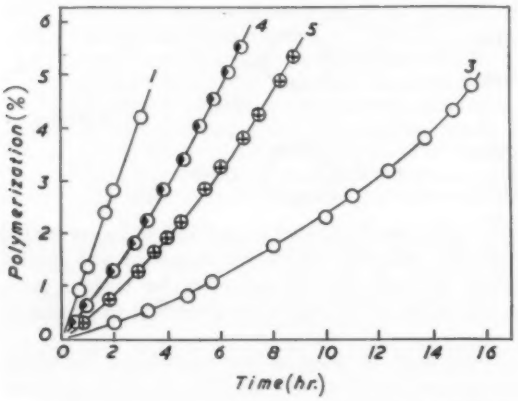


FIG. 1. *Conversion–time plots for sensitized polymerization of styrene at 60° in the presence of various concentrations of retarder* (I). *Curves are labelled with experiment numbers as in Tables 2 and 3.*

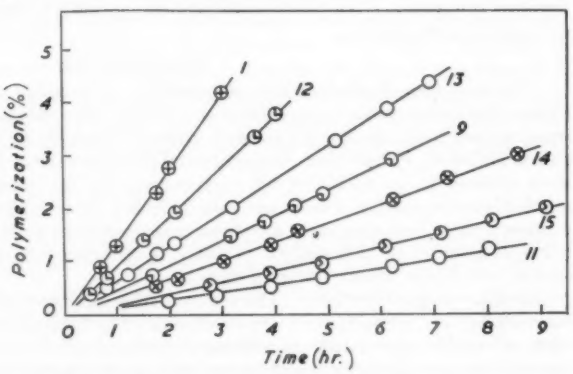


FIG. 2. *Conversion–time plots for sensitized polymerization of styrene at 60° in the presence of various concentrations of retarder* (II).

TABLE 2. *Labelled initiator, unlabelled retarder.*

Expt. no.	Initiator concn. (g./l.)	Retarder concn. (g./l.)	Rate (%/hr.)	Conversion (%)	M	c./min. for polymer	N_i
1	0·300	0	1·37	5	264,000	200	2·03
2	0·300	0·102	*	6	117,500	287	1·30
3	0·300	0·203	*	6·5	72,000	395	1·09

* Acceleration during polymerization. c./min. for initiator = 500,000.

TABLE 3. *Labelled retarder, unlabelled initiator.*

Expt. no.	Initiator concn. (g./l.)	Retarder concn. (g./l.)	Rate	Conversion (%)	M	c./min. for polymer	N_r
4	0·297	0·052	*	6·7	187,000	22	0·31
5	0·298	0·101	*	6·2	105,500	54	0·43
6	0·300	0·150	*	6	94,500	62	0·45

* Acceleration during polymerization. c./min. for retarder = 56,200.

Experiments with the N-*oxide* (II) *as retarder.* Similar experiments were performed (Tables 4 and 5, Fig. 2). There were no induction periods, and the rate of polymerization remained steady for at least 6% conversion. The retarder did not affect the polymerization of methyl methacrylate.

TABLE 4. *Labelled initiator, unlabelled retarder.*

Expt. no.	Initiator concn. (g./l.)	Retarder concn. (g./l.)	Rate (%/hr.)	M	c./min. for polymer	N_1
7	0·301	0·418	0·925	144,500	96	1·52
8	0·299	0·696	0·615	89,500	128	1·25
9	0·299	0·994	0·432	75,500	145	1·20
10	0·305	1·310	0·378	68,000	143	1·06
11	0·299	2·280	0·172	—	361	—

c./min. for initiator = 176,000.

TABLE 5. *Labelled retarder, unlabelled initiator.*

Expt. no.	Initiator concn. (g./l.)	Retarder concn. (g./l.)	Rate (%/hr.)	M	c./min. for polymer	N_r
12	0·298	0·406	0·915	151,000	90	0·36
13	0·300	0·752	0·667	99,000	166	0·44
14	0·306	1·510	0·369	58,000	338	0·52
15	0·300	2·000	0·210	44,000	475	0·55

c./min. for retarder = 161,000.

In expt. 16, an air-free solution of [^{14}C]azo*iso*butyronitrile (5·37 mg.) and the N-oxide (II) (26 mg.) in benzene (6 c.c.) was kept at 60° for 20 hr. It was then found by isotope dilution analysis that the solution contained 0·12 mg. of *iso*butyronitrile and 0·40 mg. of tetramethylsuccinodinitrile. If the N-oxide (II) had been absent from the reaction mixture, the expected yields of the nitrile and dinitrile would have been 0·40 mg. and 1·25 mg. respectively.[8]

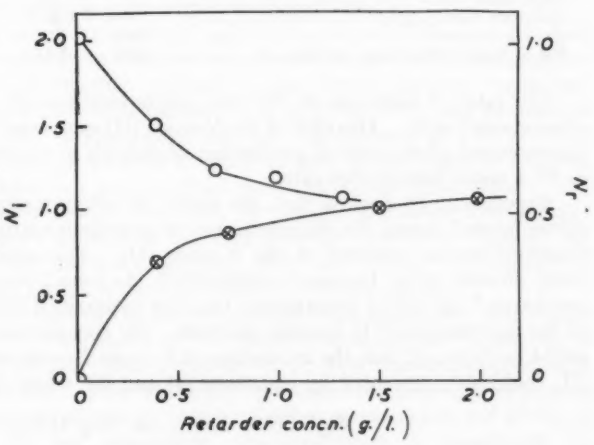


FIG. 3. *Variation of number of combined initiator fragments* ○ *and combined retarder molecules* ⊗ *in each polymer molecule with concentration of retarder.*

DISCUSSION

The results in Fig. 1 show that the hydrazine (I) retards the polymerization of styrene. The retarder is not ideal, however, since the rate of polymerization gradually rises during reaction. Comparison of the results in Tables 2 and 3 shows that as the initial concentration of retarder is increased the number of initiator fragments combined in each polymer molecule falls towards 1; at the same time the corresponding number of retarder molecules rises to a value of about 0·5. These results would satisfy the mechanism implied in

[8] Bevington, *J.*, 1954, 3707.

equations 2 and 3, but they may be misleading since the concentration of retarder in the reaction mixture evidently falls appreciably during the reaction. Further, it is unlikely that the scavenging action of diphenylpicrylhydrazyl can be represented adequately as a simple combination between the hydrazyl and the radical.

The *N*-oxide (II) appears to be more satisfactory than the hydrazine (I); the rate of reaction remains steady over an appreciable extent of polymerization (Fig. 2), but as it does not retard polymerization of methyl methacrylate it cannot be of general application.

Results in Tables 4 and 5 have been used to construct Fig. 3. The numbers of combined initiator fragments and retarder molecules show the same trend as for the hydrazine (I), and again would be satisfied by eqns. (2) and (3). The *N*-oxide (II) might be used for measuring kinetic chain lengths and rates of initiation in at least some radical polymerizations; sufficient retarder to suppress all mutual termination of reaction chains would be needed. The kinetic chain length (ν) would be half the number of monomer units combined with one retarder molecule; for styrene,

$$\frac{\text{Counting rate for polymer}}{\text{Counting rate for retarder}} = \frac{18}{18 + 16\nu}$$

The retarder might react not only with growing polymer radicals but also with the primary radicals. If so, the rate of initiation measured with the retarder would be lower than the rate of production of radicals and also lower than the rate of initiation in a system not containing the retarder but otherwise identical. This possibility was examined by comparing the rates of initiation in those experiments involving labelled initiator and unlabelled retarder (Table 6); for all these experiments, the concentration of initiator was close to 0·300 g./l.

TABLE 6.

Expt. no.	1	7	8	9	10	11
Retarder concn. (g./l.)	0	0·418	0·696	0·994	1·310	2·280
ν	1250	917	687	607	615	244
$10^8 \times$ Rate of initiation (mole/l./sec.)	2·55	2·34	2·08	1·65	1·42	1·64

The rates of initiation of retarded polymerizations are appreciably lower than those of unretarded ones. Therefore if the *N*-oxide (II) were used in conjunction with styrene for measurement of the rate of production of radicals in a system, it would be possible only to fix a lower limit to this rate.

Experiment 16 showed that the yields of *iso*butyronitrile and tetramethylsuccinodinitrile formed during the decomposition of azo*iso*butyronitrile in benzene are appreciably decreased by the presence of the *N*-oxide (II). This result demonstrates that (II) can react directly with 1-cyano-1-methylethyl (2-cyano-2-propyl) radicals. It was shown previously [6] by similar experiments that the hydrazine (I) interferes in the decomposition of the azo-compound in benzene solution. By consideration of equations (2) and (3), it might be expected that the interaction of 1-cyano-1-methylethyl radicals and the *N*-oxide (II) could be represented by equations (4) and (5), where X represents the radical (VI).

$$Me_2\dot{C}\cdot CN + X\cdot H \longrightarrow Me_2CH\cdot CN + X\cdot \quad . \; . \; . \; . \; . \quad (4)$$

$$Me_2\dot{C}\cdot CN + X\cdot \longrightarrow Me_2CX\cdot CN \quad . \; . \; . \; . \; . \; . \; . \; . \quad (5)$$

Appreciable quantities of *iso*butyronitrile would then be expected in the reaction mixture, but this was not so. This result makes it uncertain that equations (2) and (3) accurately represent the mechanism of the retardation.

It is concluded that the *N*-oxide (II) can be used to measure rates of initiation in the polymerization of styrene, so long as enough retarder is used to suppress all mutual termination of reaction chains; at 60° for an unretarded rate of 1·4%/hr., which corresponds to a rate of initiation of about $2{\cdot}5 \times 10^{-8}$ mole/l./sec., *ca.* 1·5 g./l. is adequate. The

kinetic chain length is then the number of monomer units equivalent to 0·5 molecule of *N*-oxide (II) incorporated in the polymer. For analysis of the polymer, it is necessary to use a tracer technique; if gas counting or other sensitive method of assay is used, the specific activity of the retarder (II) could be as low as about 10 μc/g. In view of the uncertainties referred to, this procedure must be regarded as empirical.

The authors thank Sir Harry Melville, F.R.S., for his interest, and the University of Birmingham for a University Research Fellowship (to N. A. G.).

CHEMISTRY DEPARTMENT, BIRMINGHAM UNIVERSITY.
CHEMICAL ENGINEERING DEPARTMENT,
ALEXANDRIA UNIVERSITY.

[*Received, December 23rd*, 1957.]

---

457. *Organic Fluorine Compounds. Part IX.* The Preparation of Fluoroacetone and 1 : 3-Difluoroacetone.*

By ERNST D. BERGMANN and SASSON COHEN.

Satisfactory procedures for these preparations are described.

NONE of the methods of preparing fluoroacetone [1] lends itself to large-scale preparations, so other methods have been studied. Attempts to fluorinate the ethylene ketals of chloro- or bromo-acetone with potassium fluoride in glycols, acetamide, or nitrobenzene failed, as did reaction of dimethylcadmium with fluoroacetyl chloride (cf. the unreactivity of fluoroacetyl chloride towards Grignard reagents [2]). Oxidation of 1-fluoro-2-methylpropan-2-ol by means of hydrogen peroxide in the presence of ferrous ion [3] gave promising results, but its usefulness was limited by the fact that the preparation of this alcohol by the action of hydrogen fluoride on *iso*butene oxide [4] or by reaction between ethyl fluoroacetate and methylmagnesium bromide gave unsatisfactory yields.

Fluoroacetone is best prepared by chromic acid oxidation of 1-fluoropropan-2-ol, which is obtained more conveniently by fluorination of commercial 1-chloropropan-2-ol with potassium fluoride by Hoffmann's method [5] than from propene oxide and hydrogen fluoride.[4] The overall yield of fluoroacetone is only 16—20%, but as much as 1 mole can be prepared at a time. α-Fluoropropionic acid was isolated as a by-product; this was attributed at first to the presence of as much as 25% of the isomeric 2-chloropropan-1-ol in the chloropropanol, but pure material gave exactly the same result. One must assume that 1-chloropropan-2-ol is converted by potassium fluoride into propene oxide which then adds hydrogen fluoride in the two possible directions. Indeed, the product always contains a certain amount of propene oxide, and Smith [6] has found that this compound also surprisingly adds hydrogen chloride in both directions.

Both 1-fluoropropan-2-ol and fluoroacetone give constant-boiling mixtures with water.

For the preparation of 1 : 3-difluoroacetone [7] 1 : 3-difluoropropan-2-ol [5] appeared to be the starting material of choice. The reaction of 1 : 3-dichloropropan-2-ol with potassium fluoride gave low yields. However, refluxing epichlorohydrin with potassium hydrogen fluoride in diethylene glycol gave 39% of 1 : 3-difluoropropan-2-ol and 17·5% of 1-chloro-3-fluoropropan-2-ol. In our experience, epichlorohydrin is unaffected by

* Part VIII, *Chem. and Ind.*, 1957, 394.

[1] Ray, Goswami, and Ray, *J. Indian Chem. Soc.*, 1935, **12**, 93; Fukuhara and Bigelow, *J. Amer. Chem. Soc.*, 1941, **63**, 788; E. D. Bergmann and Ikan, *Chem. and Ind.*, 1957, 394; Knuyants, Kisel, and Bykhovskaya, *Isvest. Akad. Nauk. S.S.S.R., Otdel. Khim. Nauk*, 1956, 377; Fraser, Millington, and Pattison, *J. Amer. Chem. Soc.*, 1957, **79**, 1959; Olah and Kuhn, *Chem. Ber.*, 1956, **89**, 864.
[2] Howell, Scott, and Pattison, *J. Org. Chem.*, 1957, **22**, 255.
[3] Merz and Waters, *J.*, 1949, 15.
[4] Knuyants, Kil'disheva, and Petrov, *Zhur. obshchei Khim.*, 1949, **19**, 95, 101.
[5] Hoffmann, *J. Amer. Chem. Soc.*, 1948, **70**, 2596.
[6] Smith, *Z. physik. Chem.*, 1918, **93**, 59.
[7] McBee, Pierce, Kilbourne, and Wilson, *J. Amer. Chem. Soc.*, 1953, **75**, 3152.

XUM

potassium fluoride in diethylene glycol; Olah and Pavlath [8] claim the formation of epifluorohydrin by this method, but Pattison and Norman [9] had to use prolonged heating of epichlorohydrin with potassium fluoride in an autoclave in order to bring about the halogen exchange. We assume, therefore, that the first step in the reaction between epichlorohydrin and potassium hydrogen fluoride is the opening of the epoxide ring by hydrogen fluoride to yield the chlorofluoropropanol which in turn, gives rise to 1 : 3-difluoropropan-2-ol. Dehydrohalogenation of 1-chloro-3-fluoropropan-2-ol yields only epifluorohydrin.

Oxidation of the halogeno-alcohols with chromic acid yields 1 : 3-difluoroacetone and 1-chloro-3-fluoroacetone. Both ketones failed to give dinitrophenylhydrazones and their semicarbazones proved unstable. Analogous observations have been made for 1 : 3-dichloroacetone.[10] Difluoroacetone, like the monofluoro-compound, gives with water a constant-boiling mixture.

After this study had been completed, Kitano and Fukui [11] claimed that fluoroacetone is formed in 66% yield from chloroacetone and potassium fluoride in ethylene glycol and that 1 : 3-difluoropropan-2-ol is obtained from 1 : 3-dichloropropan-2-ol and potassium fluoride. As the original Japanese paper was not available and, therefore, the exact operating conditions are not known to us, we cannot account for the fact that we were unable to carry out these reactions.

Experimental

1-Fluoro-2-methylpropan-2-ol.—To a solution of methylmagnesium bromide [from magnesium (24 g.), methyl bromide (110 g.), and ether (500 c.c.)], ethyl fluoroacetate (53 g.) in ether (100 c.c.) was added with stirring during 90 min. at 0—5°. The mixture was decomposed with ice and hydrochloric acid, and the ethereal solution separated, washed with dilute sodium hydrogen carbonate solution, dried (Na_2SO_4), and fractionated. The fraction (19 g.) boiling from 85° to 105° was redistilled; it had b. p. 96—98°, n_D^{28} 1·3895 (15 g., 32%) (lit.,[4] b. p. 58°/82 mm., n_D^{20} 1·3913) (Found: C, 52·3; H, 9·9. Calc. for C_4H_9OF: C, 52·2; H, 9·8%).

Fluorination of 1-Chloropropan-2-ol.—The technical chlorohydrin (336 g.) (Eastman), containing 25% of 2-chloropropan-1-ol, was added dropwise to a stirred mixture of potassium fluoride (310 g.), ethylene glycol (280 g.), and diethylene glycol (80 g.), at 170—180°. The fluorinated material was allowed to distil through a downward condenser, the temperature at the still head being maintained at 100—110° by controlling the rate of addition of the chlorohydrin. The crude distillate (165 g.), on redistillation in an efficient column, gave the following fractions: (*a*) Propylene oxide (23 g.), b. p. 34—40°; (*b*) 1-fluoropropan-2-ol (128 g., 46%), b. p. 95—110°. Fraction (*b*) was redistilled, to give the fluorohydrin (103 g., 37%), b. p. 103—105°, n_D^{20} 1·3718 (lit.,[4] b. p. 107—108°, n_D^{20} 1·3822) (Found: C, 44·7; H, 9·2. Calc. for C_3H_7OF: C, 44·9; H, 9·1%).

When the chlorohydrin, b. p. 124—128°, prepared from propylene oxide and hydrochloric acid, or pure 1-chloropropan-2-ol, prepared from allyl chloride and sulphuric acid,[6] was used in this preparation, very similar results were obtained.

Fluoroacetone.—To a stirred mixture of crude fluorohydrin, b. p. 95—110° (144 g.), sodium dichromate dihydrate (340 g.), and water (180 c.c.), a mixture of sulphuric acid (260 c.c.) and water (144 c.c.) was added during 3—4 hr., the temperature being kept at 20—25°. The mixture was diluted with water (100 c.c.) and distilled, finally for a few minutes after the temperature at the still head had reached 100°. The fluoroacetone in the distillate was salted out with sodium chloride, separated, dried ($CaCl_2$), and redistilled. It (60 g., 43%) had b. p. 78—79°, n_D^{20} 1·3627 (lit.,[1] b. p. 72·5°, 78°, 77—79°, n_D^{20} 1·3693), $\nu_{max.}$ (liquid) 1721 cm. (C=O). The dinitrophenylhydrazone had m. p. 134—135° (from ethanol) (lit., 118—119°,[1] 132° [11]) (Found: C, 41·9; H, 3·7. Calc. for $C_9H_9O_4N_4F$: C, 42·2; H, 3·5%).

Extraction of the oxidation mixture with ether, drying of the ethereal solution (Na_2SO_4),

[8] Olah and Pavlath, *Acta Chim. Hung.*, 1953, **3**, 431.
[9] Pattison and Norman, *J. Amer. Chem. Soc.*, 1957, **79**, 2311.
[10] von Romburgh, *Verslag Akad. Wetenschapp. Amsterdam*, 1922, **31**, 655.
[11] Kitano and Fukui, *Kogyo Kagashu Zasshi*, 1956, **59**, 395; *Chem. Abs.*, 1957, **51**, 11,282.

removal of the solvent, and distillation of the residue under reduced pressure, gave α-fluoropropionic acid (9 g.), b. p. 82—83°/30 mm., n_D^{26} 1·3810 (lit.,[12] b. p. 60°/5—8 mm.) (Found: C, 38·5; H, 5·2. Calc. for $C_3H_5O_2F$: C, 38·2; H, 5·4%).

1 : 3-*Difluoropropan-2-ol.*—1 : 3-Dichloropropan-2-ol (203 g.) was added dropwise to a stirred mixture of potassium fluoride (270 g.), ethylene glycol (250 g.), and diethylene glycol (80 g.) at 190—200°, as described for the chlorohydrin. The product was distilled at 130—140°. Redistillation gave the following fractions after a small fore-run: (*a*) 1 : 3-difluoropropan-2-ol (10 g.), b. p. 50—60°/34 mm., and, upon redistillation, 54—55°/34 mm. (6·5 g., 4·3%), n_D^{28} 1·3745 (lit.,[4] b. p. 59°/40 mm., n_D^{20} 1·380) (Found: C, 37·3; H, 6·2. Calc. for $C_3H_6OF_2$: C, 37·2; H, 6·2%); (*b*) 1-chloro-3-fluoropropan-2-ol, b. p. 64—65°/34 mm. (6 g., 4%), n_D^{28} 1·4141 (lit.,[4] b. p. 153—156°, n_D^{20} 1·4360) (Found: C, 32·1; H, 5·5. Calc. for C_3H_6OClF: C, 32·0; H, 5·3%).

Reaction between Epichlorohydrin and Potassium Hydrogen Fluoride.—A stirred mixture of epichlorohydrin (500 g.), potassium hydrogen fluoride (Baker and Adamson) (470 g.), and diethylene glycol (500 g.) was heated under reflux for 2·5 hr. (oil-bath, 160—170°). The mixture was allowed to cool, and the material distilled under reduced pressure, both condenser and receiver being cooled with ice-water. The distillate (325 g.), b. p. 40—80°/30 mm., upon redistillation through an efficient column, gave a fore-run (7 g.), b. p. 90—124°, 1 : 3-difluoropropan-2-ol (182° g., 36%), b. p. 124—134°, and upon redistillation (154 g., 30%), b. p. 127—128°, n_D^{28} 1·3737 (Found: C, 37·0; H, 6·2. Calc. for $C_3H_6OF_2$: C, 37·2; H, 6·2%), and 1-chloro-3-fluoropropan-2-ol (100 g., 17·5%), b. p. 135—155°, and upon redistillation, 146—148°, n_D^{28} 1·4269.

When epichlorohydrin was added dropwise to a stirred mixture of potassium fluoride and diethylene glycol or potassium fluoride and glycerol, as described above, and at a temperature as high as 220° (oil-bath), it was recovered in 50—60% yield.

Dehydrochlorination of 1-Chloro-3-fluoropropan-2-ol to Epifluorohydrin.—1-Chloro-3-fluoropropan-2-ol (112·5 g.) was treated with powdered sodium hydroxide (44 g.) and ether (300 ml.) according to the method used for epichlorohydrin.[13] Epifluorohydrin distilled at 85—86°, (50 g., 66%), n_D^{28} 1·3680 (lit., b. p. 85—86°,[4] 83—84°,[9] n_D^{20} 1·373,[4] n_D^{25} 1·3679 [9]) (Found: C, 47·3; H, 6·7. Calc. for C_3H_5OF: C, 47·3; H, 6·6%).

1 : 3-*Difluoroacetone.*—To a stirred mixture of 1 : 3-difluoropropan-2-ol (b. p. 124—130°) (60 g.), sodium dichromate dihydrate (84 g.), and water (50 c.c.), a mixture of concentrated sulphuric acid (120 g.) and water (30 c.c.) was added during 3—4 hr. at 15—20°. The mixture was stirred for 2 hr., diluted with water (200 c.c.), and distilled until about 170—200 c.c. of distillate had collected, the portion of the distillate at 97—98° containing most of the ketone. Excess of calcium chloride was added to the distillate until the ketone was salted out. This was separated, the calcium chloride solution extracted once with ether, and the ethereal solution added to the ketone, dried ($CaCl_2$), and fractionated, giving 1 : 3-difluoroacetone (24·5 g., 42%), b. p. 124—126°/760 mm., 52—53°/30 mm., n_D^{28} 1·3719, $\nu_{max.}$ (liquid) 1750 cm.$^{-1}$ (C=O) (Found: C, 38·3; H, 4·3. Calc. for $C_3H_4OF_2$: C, 38·2; H, 4·3%). Difluoroacetone is extremely soluble in water, probably through hydrate formation, as shown by evolution of heat when it is added to water; it forms an azeotrope, b. p. 97—98°, with water. It cannot be salted out with sodium chloride or sodium sulphate, nor is it possible to extract it efficiently from water by means of ether. This makes its recovery from oxidation mixtures by means of extraction a very tedious and inefficient procedure. The *semicarbazone*, obtained from an aqueous solution, is very unstable; it cannot be purified by recrystallization; it had m. p. 143—146° (Found: C, 31·8; H, 4·9. $C_4H_7ON_3F_2$ requires C, 31·8; H, 4·6%).

2 : 2-*Di(fluoromethyl*)-1 : 3-*dioxolan.*—Since difluoroacetone could not be characterised by a stable solid derivative, and in order to differentiate it from the 1 : 3-difluoropropan-2-ol, which has a very similar b. p., a ketal was prepared: difluoroacetone (10 g.), ethylene glycol (7·0 g.), and toluene-*p*-sulphonic acid (0·25 g.) in benzene were refluxed azeotropically for 5—6 hr., about 2 c.c. of water being collected; The acid was neutralized, the solvent was removed by distillation, and the *ketal* distilled under reduced pressure (yield, 8 g., 54%; b. p. 64—65°/30 mm., n_D^{27} 1·3989) (Found: C, 44·3; H, 6·2. $C_5H_8O_2F_2$ requires C, 43·5; H, 5·8%).

Oxidation of 1-Chloro-3-fluoropropan-2-ol to 1-Chloro-3-fluoroacetone.—To a stirred mixture of the propanol, b. p. 140—150° (64 g.), sodium dichromate dihydrate (96 g.), and water (54 c.c.), a mixture of sulphuric acid (114 g.) and water (50 c.c.) was added at 20—25° during 4—5 hr. Stirring was continued for 2 hr. more, and the mixture diluted with water (250 c.c.) and distilled

[12] Gryszkiewicz-Trochimowski and Gryszkiewicz-Trochimowski, *Bull. Soc. chim. France*, 1949, 928.
[13] Clarke and Hartman, *Org. Synth.*, Coll. Vol. I, 2nd edn., p. 233.

at 70—80 mm. until about 200 c.c. of distillate had been collected. To this was added calcium chloride in excess until the ketone separated as the bottom layer. This was separated, dried ($CaCl_2$), and fractionated, to yield 1-chloro-3-fluoroacetone (29 g., 46%), b. p. 142—144°, n_D^{28} 1·4195 (lit., b. p. 141·5—143·5°,[4] 55°/20 mm.,[1] n_D^{20} 1·4277 [1]) $\nu_{max.}$ (liquid) 1754 cm.$^{-1}$ (C=O) (Found: C, 32·6; H, 3·7. Calc. for C_3H_4OClF: C, 32·2; H, 3·6%). A very unstable semicarbazone, m. p. 116—118°, was obtained from an aqueous solution of the compound.

2-Chloromethyl-2-fluoromethyl-1 : 3-dioxolan.—This *compound*, obtained (78%) from fluorochloracetone (5·5 g.), ethylene glycol (3·1 g.), and toluene-*p*-sulphonic acid (0·25 g.) as described above, had b. p. 82—84°/30 mm., n_D^{27} 1·4320 (Found: C, 38·6; H, 5·3. $C_5H_8O_2ClF$ requires C, 38·8; H, 5·2%).

This investigation was supported by a grant of The National Institutes of Health, Bethesda, Maryland (U.S.A.).

Department of Organic Chemistry, Hebrew University, Jerusalem.
Scientific Department, Israel Ministry of Defence,
Tel-Aviv, Israel. [*Received, January 6th*, 1958.]

---

458. *The Solvolysis of Acetic Anhydride in 50% Aqueous Acetone catalysed by Nitrite Ion.*

By E. B. Lees and B. Saville.

Kinetic studies have shown that the solvolysis of acetic anhydride is markedly catalysed by nitrite ions. The rate-determining step involves nucleophilic attack by nitrite ion on the anhydride molecule (specific rate constant ~9 l. mole^{-1} min.$^{-1}$) to produce an intermediate, believed to be acetyl nitrite, which undergoes relatively instantaneous decomposition in the buffered solvent to regenerate nitrite ion. Evidence for the intermediate formation of acetyl nitrite is afforded by experiments where α-naphthylamine was included in the solvolysis systems: 4-amino-1 : 1′-azonaphthalene was then formed in amounts which could be calculated on the assumption of acetyl nitrite's functioning as a nitrosating agent. A new procedure for the determination of acetic anhydride in low concentrations has been developed.

Catalytic effects in the solvolysis of acetic anhydride have formed the subject of several studies during the last few decades. Carboxylate ions [1] and pyridine or quinoline derivatives [2] influence it and their effects have been quantitatively investigated. Catalysis by these bases can usually be ascribed to the formation, by nucleophilic attack of the catalyst on the anhydride carbonyl group, of a very easily hydrolysable intermediate which rapidly regenerates the catalyst. Catalysis by acetate ion [1] cannot be interpreted by a similar scheme and one may assume that in this case Brönsted-type classical base-catalysis is responsible. Catalysis by nitrite ions has however not been recorded, though Liddell and Saville [3] show that nitroso-compounds were formed when acetic anhydride was added to an acetate-buffered solution of sodium nitrite and an aromatic amine in aqueous acetone. The present paper deals with the action of nitrite ion upon acetic anhydride in aqueous acetone, in both the presence and the absence of α-naphthylamine as nitrosatable substrate.

Experimental

Materials.—" AnalaR " acetic anhydride was redistilled through a helix-packed column, and the fraction boiling at 139·1°/743 mm. collected. Acetone was purified by refluxing it over potassium permanganate for several days before final distillations. " AnalaR " α-naphthylamine was purified by several recrystallisations of its hydrochloride from water and liberation

[1] Kilpatrick, *J. Amer. Chem. Soc.*, 1928, **50**, 2891.
[2] Bafna and Gold, *J.*, 1953, 1406; Gold and Jefferson, *J.*, 1953, 1409.
[3] Liddell and Saville, *Chem. and Ind.*, 1957, 493.

XUM

of the free base, which was distilled. It had m. p. 49° and contained no β-isomer as judged by chromatography on alumina with toluene as eluent, or by chromatography of the dye formed by coupling with diazotised *m*-chloroaniline: mixtures of the α- and β-isomers could be separated by these techniques.

" AnalaR " sodium acetate and sodium nitrite were used as supplied, after drying for several hours in a vacuum-oven.

Determination of Acetic Anhydride.—This was done colorimetrically by a new procedure based on the principle described by Liddell and Saville.[3] Calibration was by adding 1 ml. of a stock solution of acetic anhydride (0·0001—0·0013M) in acetone to about 20 ml. of reagent A contained in a 25 ml. volumetric flask. [The reagent A is made up as required by mixing 20 ml. of N-sodium nitrite and 80 ml. of N-sodium acetate (both aqueous) with 100 ml. of 0·006M-α-naphthylamine solution in acetone. It is important to keep this reagent from strong daylight. Determinations of acetic anhydride were performed in a dark corner of the laboratory; there the reagent could be used for at least 2—3 hr.] The contents of the flask were made up to the mark with further reagent A, mixed, and set aside for 15—20 min., the intensity of the resultant orange-coloured solution being measured on a Hilger " Spekker " absorptiometer with 601 filters and 1 cm. cells. Reagent A was used as the control.

There existed a linear relation between absorptiometer readings (*S*) and the anhydride concentrations in the stock solutions. Up to 100 times the concentration of acetic acid did not interfere. Typical results are presented in Table 1.

TABLE 1. *Determination of acetic anhydride with reagent A.*

[Acetic anhydride] (10^{-4} mole/l.)	2·5	5·0	7·5	10	12·5
S	0·151 ±0·001	0·302 ±0·001	0·454 ±0·002	0·608 ±0·002	0·761 ±0·003

Rate of Decomposition of Acetic Anhydride in Aqueous Acetone.—To check the validity of the above procedure for anhydride determinations when applied to kinetic measurements, the rates of hydrolysis of acetic anhydride in several aqueous-acetone solvents were measured as follows.

To the solvent (100 ml.) in a stoppered flask, which had been brought to 25° in a thermostat, was added 0·1M acetic anhydride (in acetone) (1 ml.). Aliquot parts (1·00 ml.) were withdrawn with a calibrated tuberculin syringe and added at recorded times to about 20 ml. of reagent A and made up to 25 ml. with further reagent A, further procedure being as described above.

First-order plots of excellent linearity were obtained by plotting $\log_{10} S$ against time, from which the first-order rate constants k_0 were calculated in the conventional manner.

In Table 2 these rate constants are compared with Gold's results,[4] the good agreement indicating that the new procedure is satisfactory for anhydride determinations in kinetic runs.

TABLE 2. *First-order rate constants (k_0) for hydrolysis of acetic anhydride in aqueous acetone at 25°.*

Acetone (wt. %) in solvent	0	20	30	50
k_0 (min.$^{-1}$), this work	0·1495	0·0510	0·0252	0·00584
Gold's work	0·1575	0·0520	0·0265	0·00587

Effect of Nitrite-ion Concentration on the Rate of Hydrolysis of Acetic Anhydride in 50% (v/v) Aqueous Acetone.—Stock 1·00M-solutions of sodium nitrite and sodium acetate in 50% (v/v) aqueous acetone were mixed with extra solvent to produce several solutions ranging from 0·1 to 0·5M in sodium acetate and 0·005 to 0·040M in sodium nitrite. The acetate ion was present to buffer the effect of acetic acid liberated in the anhydride hydrolysis which might otherwise reduce the effective nitrite-ion concentration during reaction.

100 ml. of these acetate–nitrite solutions at 25° were used and the rate of decomposition of added acetic anhydride (initial concentration 0·001M) was followed as just described. The rates were found to be of strictly first order with respect to the anhydride, and the values of the constants were calculated graphically in the usual manner.

Reaction of Acetic Anhydride with Acetate–Nitrite Solutions in the Presence of α-Naphthylamine.—The almost quantitative formation of 4-amino-1 : 1′-azonaphthalene from acetic anhydride, excess of sodium acetate, sodium nitrite, and α-naphthylamine in aqueous acetone

[4] Gold, *Trans. Faraday Soc.*, 1948, **44**, 506.

XUM

was observed as follows: To sodium acetate (41 g., 0·5 mole) and sodium nitrite (6·9 g., 0·1 mole) in water (500 ml.) was added α-naphthylamine (14·3 g., 0·1 mole) in acetone (450 ml.). The solution was cooled, and acetic anhydride (1·02 g., 0·01 mole) in acetone (50 ml.) added with stirring which was continued for 30 min., before extraction with chloroform (3 × 150 ml.). The combined extracts were washed with three equal volumes of water, dried, and evaporated under reduced pressure. The residue was taken up in toluene (100 ml.), and concentrated hydrochloric acid (10 ml.) added. The mixture was shaken vigorously and the solid hydrochlorides were filtered off, washed with a little acetone, and suspended in N-hydrochloric acid (300 ml.) at 50°. The naphthylamine hydrochloride dissolved, leaving the crude dye hydrochloride which was filtered off and shaken with aqueous ammonia and chloroform to extract the free base. The extracts were dried and evaporated, yielding the crude dye which was recrystallised from benzene–light petroleum (b. p. 60—80°). 4-Amino-1 : 1′-azonaphthalene (2·77 g., 93·6% based on anhydride) was obtained, with m. p. and mixed m. p. 184—185° (Found: C, 80·6; H, 5·2. Calc. for $C_{20}H_{15}N_3$: C, 80·8; H, 5·1%).

Kinetics of Azo-dye Formation.—Aqueous-acetone solutions containing α-naphthylamine, sodium nitrite, sodium acetate, and acetic acid were prepared from stock solutions of each component. 100 ml. portions of these solutions (at 25°) were treated with M/100-acetic anhydride (1·00 ml.) in acetone, and 5 ml. portions then added to N-ammonia in 50% aqueous acetone (20 ml.) to stop the reaction (excess of anhydride is decomposed instantaneously) and the intensity of colour was measured as before except that 3·0 cm. cells were used.

S_∞ being the reading at completion of the reaction (taken at ten half-lives), and S_t a reading at time t, plots of $\log_{10}(S_\infty - S_t)$ against time gave very good straight lines from which first-order constants were obtained. It had been previously demonstrated that the relation between azo-dye concentration and absorptiometer reading was linear.

Results and Discussion

The first-order rate constants for decomposition of acetic anhydride bore a linear relation to both acetate- and nitrite-ion concentration. Thus the relation $k_0 = k_H + k_1[AcO^-] + k_2[NO_2^-]$ is obeyed where k_H is the first-order rate constant for the uncatalysed reaction and k_1 and k_2 are the respective catalytic coefficients (in l. mole^{-1} min.$^{-1}$) for acetate and nitrite ions.

The value of k_H was found by studying the hydrolysis of the anhydride in 50% aqueous acetone in the absence of other substances. The effect of added acetate ion on the decomposition rate in the absence of nitrite ion allows k_1 to be calculated, and the value of k_2 was found by plotting k_0 against nitrite-ion concentration at constant acetate concentration. Results are summarised in Table 3.

Table 3. *The effect of nitrite- and acetate-ion concentration on the first-order rate constants (k_0) for the decomposition of acetic anhydride (initially 0·001M) in 50% aqueous acetone at 25°.*

	NaOAc 0·100		NaOAc 0·200		NaOAc 0·500 mole l.$^{-1}$	
[$NaNO_2$] (mole l.$^{-1}$)	k_0 (min.$^{-1}$)	Mean k_2 *	k_0 (min.$^{-1}$)	Mean k_2 *	k_0 (min.$^{-1}$)	Mean k_2 *
0·000	0·0203		0·0305		0·0603	
0·005	0·0645		0·0770		0·106	
0·010	0·109	8·85	0·124	9·25	0·150	9·35
0·020	0·198		0·216		0·247	
0·030	0·286		0·308		0·340	

In absence of $NaNO_2$ and NaOAc, k_0 (= k_H) = 0·0110 min.$^{-1}$.
Mean calc. value of k_1 = 0·0986 l. mole^{-1} min.$^{-1}$.
* l. mole^{-1} min.$^{-1}$.

The fact that nitrite ion functions purely as a catalyst in these reactions was established in two ways. Some runs were performed with 0·01M-nitrite and 0·2M-acetate with initial concentrations of 0·01M- and 0·02M-acetic anhydride. When the concentration of acetic anhydride in the system had fallen to about 0·001M measurements on the rate of decomposition were commenced. The rate constants thus obtained were only very slightly lower

than that recorded in Table 3, indicating very little loss of nitrite from the systems. Table 4 gives this comparison.

TABLE 4. *Rate data for decomposition of acetic anhydride in* 0·2M-*acetate plus* 0·01M-*nitrite in* 50% *aqueous acetone at* 25°.

Initial $[Ac_2O]$ (mole $l.^{-1}$)	0·001	0·010	0·020
Final decompn. rate, k_0 ($min.^{-1}$)	0·124	0·118	0·111

Determination of the residual nitrite concentration after reaction with acetic anhydride indicated that even in the system where the initial anhydride concentration was double the nitrite concentration, the latter was reduced to only some 92% of its original value. In a purely aqueous system there was no overall utilisation of nitrite at all, even after the reaction with a ten-fold excess of anhydride.

The rate of decomposition of acetic anhydride in these systems can be accurately defined by the equations

$$-d[Ac_2O]/dt = k_0[Ac_2O]$$

and

$$k_0 = k_H + k_1[AcO^-] + k_2[NO_2^-]$$

where the last term refers to the nitrite-catalysed hydrolysis.

Since the rate of the latter process, in which we are primarily interested, is directly proportional to the nitrite-ion concentration it seems that one could set up a crude mechanistic interpretation of this reaction by postulating that nitrite ion attacks acetic anhydride in a bimolecular rate-controlling step to yield some intermediate which decomposes relatively instantaneously producing acetic acid and nitrite ion which is then available for participation in further reactions:

$$O{\cdot}NO^- + Ac_2O \xrightarrow[\text{Slow}]{k_2} \text{Intermediate} \xrightarrow[\text{Fast}]{H_2O} O{\cdot}NO^- + 2AcOH$$

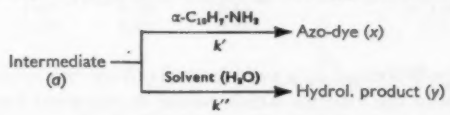
k_2 then becomes the second-order rate constant for the slow step.

The existence of the intermediate would be substantiated if some substance included in the system competed with the solvent molecules (water) for the intermediate to produce an easily recognisable product. Now, addition of α-naphthylamine to the nitrite–acetic anhydride reaction led to the formation of 4-amino-1 : 1′-azonaphthalene (referred to below as " azo-dye "). Correspondence between the amounts of this dye produced and the calculated fraction of intermediate which could be formed if its hydrolysis were avoided, and the kinetics of azo-dye formation, were in fact consistent with existence of the intermediate.

TABLE 5. *Effect of* α-*naphthylamine concentration on azo-dye formation from* 0·1M-*nitrite and* 0·4M-*acetate in* 50% *aqueous acetone after reaction of* 0·00004M-*acetic anhydride at* 25° *for* 20 *minutes.*

[α-Naphthylamine] (10^{-4} mole $l.^{-1}$)	1·25	2·5	5·0	12·5	25	50	100
Mole ratio of azo-dye formed to Ac_2O used	0·420	0·561	0·710	0·909	0·924	0·924	0·911

In solutions where the acetate and the nitrite ion were in effectively constant excess over the initial anhydride, the final ratio of dye formed to anhydride used varied with initial α-naphthylamine concentration as shown, for example, in Table 5. If the azo-dye is produced by competition of the α-naphthylamine with solvent for the intermediate, the theory of competing first-order reactions can be applied to the scheme:



where x and y are the respective final concentrations of the azo-dye and hydrolysis products,

a is the initial concentration of intermediate, and k' and k'' are the first-order rate constants for the two competing reactions; this leads to the expression:

$$a/x = (k''/k')[\alpha\text{-}C_{10}H_7\cdot NH_2] + 1 \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where $$k[\alpha\text{-}C_{10}H_7\cdot NH_2] = k'$$

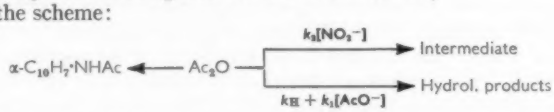
This has been tested graphically by plotting a/x (inverse of row 2 in Table 5) against the reciprocal of the amine concentration. A straight line results, from the slope of which one obtains a value of $k''/k = 1{\cdot}54 \times 10^{-4}$. α-Naphthylamine at this concentration ($1{\cdot}54 \times 10^{-4}$M) competes on equal terms with the solvent for the intermediate. Since the azo-dye must be formed from two molecules of α-naphthylamine but the kinetics of its formation from the intermediate are of the first order in amine concentration, it appears that a subsequent even faster step is involved whereby the primary reaction product of intermediate and α-naphthylamine reacts with another molecule of α-naphthylamine.

Very probably the complete decomposition of the intermediate can be represented, thus: *

This scheme requires that the rate of azo-dye formation from the intermediate is of the first order in α-naphthylamine, as observed experimentally.

Let it now be supposed that the intermediate does not decompose in the solvent, and consider what hypothetical relation exists between the final intermediate concentration and the initial anhydride concentration. (This is one way, in fact, of calculating what fraction of the anhydride decomposes *via* the intermediate.)

In terms of the scheme:



the expression for the final intermediate concentration becomes

$$[\text{Intermediate}] = [Ac_2O]k_2[NO_2^-]/k_d \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where k_d is the total decomposition rate $= k_H + k_1[AcO^-] + k_2[NO_2^-] + k_N$ and k_N is the first-order rate constant for α-naphthylamine acetylation, which has the value 0·023 min.$^{-1}$ for 0·005M-α-naphthylamine. The very good agreement between calculated intermediate and azo-dye concentrations shown in Table 6 again confirms the reaction mechanism postulated.

TABLE 6. *Formation of azo-dye in reaction of* 0·005M-α-*naphthylamine, varying nitrite concentrations,* 0·0001M-*acetic anhydride,* 0·02M-*acetate, and* 0·005M-*acetic acid in* 50% *aqueous acetone, and the concentration of intermediate calculated from equation* 2.

[Nitrite] (mole l.$^{-1}$)	0·005	0·010	0·020	0·030	0·040
[Intermediate] (10^{-6} mole l.$^{-1}$)	44·5	61·4	76·1	82·2	86·4
[Azo-dye] (mole l.$^{-1}$) (±1%)	43·2	59·3	75·7	82·7	86·4

Finally, if the azo-dye is formed in a very fast step from the intermediate, the kinetics of dye formation are really the kinetics which would be observed for the formation of the

* All processes are assumed to be very fast compared with the rate of formation of the intermediate.

XUM

intermediate if the latter could be preserved from subsequent reaction. Kinetic analysis of the system:

$$\underset{(\beta)}{\text{Intermediate}} \xleftarrow{k_2[NO_2^-]} \underset{(\alpha-\beta-\gamma)}{Ac_2O} \xrightarrow{k_a} \underset{(\gamma)}{\text{Other products}}$$

where k_a is the sum of the first-order constants for alternative decomposition routes not involving nitrite reaction, α = initial[Ac_2O], and β and γ the time-variable concentrations of the respective product species, yields the expression:

$$-\log(\beta_\infty - \beta) = (k_2[NO_2^-] + k_a)t/2{\cdot}303 + \text{constant} \quad . \quad . \quad . \quad (3)$$

Since β is proportional to the dye concentration which is in turn proportional to the absorptiometer readings S it follows that the constants obtained by plotting $\log_{10}(S_\infty - S_t)$ against time (see Experimental section, rates of azo-dye formation) should equal the total rate of decomposition of the acetic anhydride, *i.e.*, $k_a + k_2[NO_2^-]$. We can also arrive at the value of $(k_a + k_2[NO_2^-])$ in another way, not presupposing an intermediate. This is by direct measurement of the rate of decomposition of the anhydride in nitrite–acetate solutions in the absence of α-naphthylamine, and adding an independently determined term for the rate of acetylation of α-naphthylamine. Table 7 indicates the excellent correspondence between acetic anhydride decomposition rates obtained (*a*) by measurement of azo-dye production and (*b*) by direct measurement of residual anhydride. The figures in the difference column are seen to be approximately constant and equal to the independently determined rate constant for the reaction between α-naphthylamine and

TABLE 7. *Rates of decomposition of acetic anhydride* (0·0001M) *in the absence and the presence of α-naphthylamine at* 25°.

	First-order rate constants (min.$^{-1}$)		
$[NO_2^-]$ (mole l.$^{-1}$)	By measurement of residual anhydride *	By measurement of azo-dye produced †	Difference
0·00	0·0434	—	—
0·005	0·0743	0·0980	0·025
0·010	0·118	0·140	0·022
0·020	0·206	0·230	0·024
0·030	0·295	0·319	0·024
0·040	0·381	0·400	0·019

* Initially, 0·20M-AcO^-, 0·005M-AcOH, 50% aqueous acetone.
† Initially, 0·20M-AcO^-, 0·005M-AcOH, 50% aqueous acetone, +0·005M-α-naphthylamine.

acetic anhydride. Both sets of measurements are linear with nitrite-ion concentration and yield 8·73 l. mole^{-1} min.$^{-1}$ for the catalytic coefficient (k_2) of nitrite ions, in satisfactory agreement with the values in Table 3.

We next discuss the chemical identity of the intermediate. The most obvious initial product from nitrite ion and acetic anhydride under non-solvolytic conditions is acetyl nitrite,[5] whole potentialities as a nitrosating agent have not been studied. One may suppose (by analogy with the nitrating properties of acetyl nitrate towards benzene [6]) that it would be able to nitrosate effectively any convenient nucleophilic centre, Z:, by the general scheme, $Z: + O{=}N{\cdot}OAc \longrightarrow Z{\cdot}N{=}O + :OAc$. Presumably both water and α-naphthylamine react in this way in the systems discussed, so that the azo-dye formation can be explained rationally in terms of the equations:

$$ON{\cdot}OAc + Ar{\cdot}NH_2 \longrightarrow Ar{\cdot}NH{\cdot}N{=}O + HOAc$$

$$\Updownarrow$$

$$Ar{\cdot}N{=}N{\cdot}OH \xrightarrow{Ar{\cdot}NH_2} \text{Dye}$$

[5] Ferrario, *Gazzetta*, 1910, **40**, II, 95; Francesconi and Cialdea, *ibid.*, 1904, **34**, I, 435.
[6] Cohen and Wibaut, *Rec. Trav. chim.*, 1935, **54**, 409.

Further to this argument we have noticed that methyl nitrite (inferred from the nitrosating properties of an organic extract) may be formed when sodium nitrite and acetic anhydride react in methanol.

It is not thought likely that heterolysis of the carbonyl–oxygen bond occurs during acetyl nitrite solvolysis. Thus, acetate ion did not significantly affect the nitrite-ion catalytic coefficient, k_2, as Table 3 shows. If acetate ion had attacked the acetyl nitrite to yield acetic anhydride, this would have led to considerable decrease of k_2, with increase of acetate-ion concentration.

There is also some indirect evidence that the acetyl nitrite may attack the acetone in our solvent. In certain cases there was a very small loss of nitrite ion from the system after reaction with excess of acetic anhydride and in these instances an extremely small quantity of cyanide was found in the final solution. The cyanide could arise from the reaction of the anhydride with hydroxyiminoacetone [7,8] which could be formed by nitrosation of the acetone by the acetyl nitrite.

The high reactivity of nitrite ions towards other reactive carbonyl centres has been checked by demonstrating that *p*-substituted benzoyl chlorides, ethyl chloroformate, and succinic and butyric anhydride also give approximately equimolar amounts of azo-dye with nitrite–acetate–α-naphthylamine solutions. This high order of nitrite-ion reactivity was expected because it had been shown that the anions of oximes [8] and hydroxamic acids,[9] which like nitrite ion contain the $-\dot{N}-O^-$ arrangement, are powerful nucleophilic reagents towards certain organophosphorylating agents, and because phosphoryl derivatives behave similarly to carbonyl compounds.[10]

These nucleophilic reagents sometimes exhibit about 1000 times the reactivity of simple buffer anions of the same basicity. The decomposition of the acylated or phosphorylated products which often occurs extremely rapidly usually involves nitrogen–oxygen bond fission in a similar manner to that postulated for decomposition of acetyl nitrite.

No satisfactory explanation has been advanced for the extremely high nucleophilicity : basicity ratio exhibited by anions of this type towards carbonyl or phosphoryl derivatives.

The authors thank Mr. H. F. Liddell for instruction in chromatographic techniques. One of them (E. B. L.) thanks the M.O.S. for the award of a vacation studentship during the tenure of which this work was performed, the other (B. S.) for a Civil Service Senior Research Fellowship.

Chemical Defence Experimental Establishment,
Porton Down, Wilts. [*Received, January 7th*, 1958.]

[7] Saville, *Analyst*, 1957, **82**, 269.
[8] Green and Saville, *J.*, 1956, 3887.
[9] Green, Sainsbury, Saville, and Stansfield, *J.*, 1958, 1583.
[10] Dostrovsky and Halmann, *J.*, 1953, 508 *et seq.*

459. *The Action of Two Antibacterial Agents on the Growth of* Bact. lactis aerogenes.

By B. J. McCarthy and Sir Cyril Hinshelwood.

A study has been made of the effect on the growth of *Bact. lactis aerogenes* of 2 : 4-dinitrophenol and of disodium dihydrogen ethylenediamine-*NNN'N'*-tetra-acetate at sub-lethal concentrations.

Over the wide range of concentrations employed the presence of this sodium salt affects only the rate of multiplication of the cells without inducing an initial lag phase, the growth rate being reduced progressively with increase in concentration. Repeated subculture at a given concentration of the toxic agent reduces the inhibitory effect but does not completely eliminate it.

On the other hand 2 : 4-dinitrophenol evokes a more usual type of response, the lag shown at a first subculture in the drug medium being rapidly eliminated. Various distinct sub-strains are developed by serial subculture at particular concentrations. The lag characteristics of any given sub-strain tested at a series of drug concentrations are quantitatively related to the concentration at which it has been trained.

The training to the drug has no detectable effect on the respiratory properties of the cells but affects their ability to undergo adaptation to new sources of carbon.

The development of drug resistance to toxic agents by a given kind of bacterium may follow very varied patterns. The adaptive response of *Bact. lactis aerogenes* to 2 : 4-dinitrophenol and to ethylenediamine-*NNN'N'*-tetra-acetic acid (E.D.T.A.) illustrates this phenomenon and is here considered in some detail.

Experimental Details and Techniques

The stock strain of *Bact. lactis aerogenes* used was maintained in " Lemco " broth, and acclimatised when required to a standard minimal medium made by mixing the following solutions: 10 ml. of aqueous glucose (50 g./l.); 10 ml. of phosphate buffer ($Na_2HPO_4,12H_2O$ 16 g./l., KH_2PO_4 2·96 g./l.; pH = 7·1); 5 ml. of aqueous ammonium sulphate (5 g./l.); 1 ml. of magnesium sulphate ($MgSO_4,7H_2O$ 1 g./l.; containing 5·2 mg. of ferrous sulphate per l.).

The two drugs used in the experiments were dissolved in the standard phosphate buffer and the pH finally adjusted by the addition of a few drops of concentrated sodium hydroxide. The appropriate amount was then added to the above medium in place of all or part of the 10 ml. of phosphate solution so as to obtain the required final concentration.

The solid agar medium consisted of the same materials with the addition of 1·25% of agar. The following amounts were dissolved in 800 ml. of glass-distilled water: $Na_2HPO_4,12H_2O$ 8·0 g., KH_2PO_4 1·5 g., $(NH_4)_2SO_4$ 0·6 g., $MgSO_4,7H_2O$ 0·05 g., agar 10·0 g.

Population changes in liquid cultures were estimated with the aid of a Hilger " Spekker " light-absorptiometer, calibrated against the microscope count of actual numbers of bacteria made in a hæmocytometer counting chamber. For these purposes samples of an actively growing log-phase glucose culture were used. With the calibration so obtained turbidimetric readings can be expressed as a number equal to the cell count, in 10^6 per ml., of a glucose culture of the same optical density. This was used in plotting growth curves for estimations of lag and mean generation time.

The Action of Disodium Dihydrogen Ethylenediamine-*NNN'N'*-Tetra-acetate

The effect of this drug on the kinetics of growth when the bacteria are subcultured for the first time into a medium containing it is rather unusual. Throughout the wide range of concentrations used, 5 to 10,000 mg./l., the cells were able to multiply without a preliminary phase of adjustment although at a rate decreasing with increasing concentration. In Fig. 1 this is shown by a plot of the mean generation time (m.g.t.) against the logarithm of the concentration. Fig. 2 gives the actual growth curves corresponding to some of these determinations.

XUM

For this series of measurements five tubes containing the E.D.T.A. salt at 0, 10, 100, 1000, and 10,000 mg./l. were inoculated in parallel with 0·1 ml. of an actively growing culture.

The Figure shows that, after division has taken place about twice, the cells begin to grow

FIG. 1. *Plot of mean generation time against log of E.D.T.A. salt concentration.*

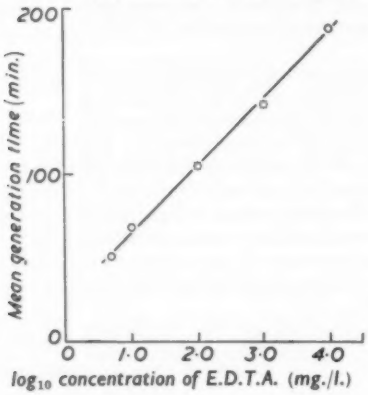
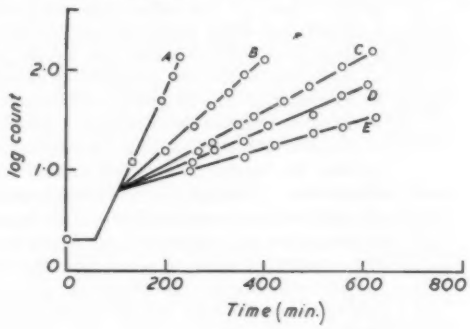


FIG. 2. *Growth curves for cultures containing (A) 0 (B) 10, (C) 100, (D) 1000, and (E) 10,000 mg. 0, E.D.T.A. salt per l.*



at a reduced rate. The dependence of this new rate of multiplication on the concentration is reflected in the fan-wise distribution of the portions of the growth curve corresponding to logarithmic growth.

Measurements were continued throughout a process of training by two series of subcultures

TABLE 1. *Training to E.D.T.A.*

Initial subculture in disodium dihydrogen ethylenediamine-*NNN'N'*-tetra-acetate		Mean generation times of successive subcultures at 10 mg./l.			
Concn. (mg./l.)	Mean generation time (min.)	No. of previous subcultures at 10 mg./l.	Mean generation times (min.) at 10 mg./l.	100 mg./l.	1000 mg./l.
0	31	0	68	105	142
5	51	5	62	—	—
10	68	9	37, 83 *	—	—
100	105	11	37, 57 *	—	—
1000	142	13	46	—	—
10000	187	17	63	—	—
		19	47	—	—
		21	50	—	—
		22	51	67	78
		23	59	—	—
		36	48	—	—
		43	50	—	—
		45	49	—	—
		59	46	—	—
		61	48	—	—
		66	46	46, 68 *	81

Mean generation times of successive subcultures at 100 mg./l.

No. of previous subcultures at 100 mg./l.	Mean generation times (min.) at 10 mg./l.	100 mg./l.	1000 mg./l.
0	68	105	142
5	—	80	—
15	—	68	—
21	51	72	77
23	—	70	—
38	—	50	—
40	47	53	80
45	—	51	—

* Composite growth curve.

carried out at concentrations of 10 and 100 mg./l. When tests were to be made the parent strain was subcultured into two tubes in parallel from one of which samples were taken at 20 min. intervals for the determination of growth rate, the second tube serving as the routine day-to-day subculture. From time to time a complete set of growth curves at drug concentrations of 0, 10, 100, and 1000 mg./l. were determined for the trained strain (Table 1).

The two Tables of mean generation times indicate clearly that training takes place. There is an apparent limit to the training process at m.g.t. values of about 46 and 51 min. for the respective strains. These figures may indeed represent an approach to the same limit, particularly in view of the fact that training at the higher concentration was carried out for a somewhat shorter period.

Prolonged growth by serial subculture was shown to be impossible at concentrations as high as 1 g./l., where the cells would not grow after the third subculture. This result is probably connected with Lodge and Hinshelwood's observation [1] that growth of *Bact. lactis aerogenes* is completely inhibited at concentrations of magnesium sulphate below 2×10^{-6} g./l. The concentration of magnesium sulphate hydrate in the standard medium is 4×10^{-2} g./l. so that at concentrations of the E.D.T.A. salt in the region of 1 g./l. the Mg^{++} concentration is probably reduced below this critical level by complex formation.

The training process does not appear to result in the ability of cells to use the drug as a source of carbon, neither of the trained strains being able to grow in a medium containing the compound as sole source. This is not to say, however, that the drug is not metabolised in some way.

The Action of Dinitrophenol

In general, phenols affect bacterial metabolism by the precipitation of proteins, which causes a general reduction in the rate of enzyme reactions within the cell,[2] but in addition to this common property some phenols have more selective actions.[3]

In the adaptation of *Bact. lactis aerogenes* subcultured in sub-lethal concentrations of phenols [4] there are two types of behaviour illustrated by the cases of phenol and thymol. In a medium containing phenol there is simply an extremely slow increase in growth rate whereas with thymol there is an elimination, after a few subcultures, of an initial very long lag. A series of alkyl phenols show intermediate behaviour. Strains resistant to increased concentrations of thymol have been obtained by continued cultivation in its presence, but, in contrast, attempts to produce strains appreciably resistant to higher concentrations of phenol proved unsuccessful.

2 : 4-Dinitrophenol has been widely used in biochemical studies since it has a specific action on certain internal cell processes. Experiments with animal-cell extracts have shown that it inhibits the assimilatory processes through which new structures are built up.[5]

The present study is concerned with the training of *Bact. lactis aerogenes* to resist increased concentrations of dinitrophenol, the mechanisms by which such resistance is acquired, and the effect of the training upon some biochemical properties of the organism. The methods used are similar to those employed in the study of the resistance of *Bact. lactis aerogenes* to proflavine and of *Saccharomyces cerevisiae* to dinitrophenol.[6]

The resistance of the cells in liquid cultures was assessed by means of lag–concentration curves. A series of tubes were prepared containing the standard growth medium and the drug at about ten appropriate concentrations. These were inoculated with 0·1 ml. volumes of the culture in or immediately after the logarithmic phase. The lags in the various media were then plotted against the drug concentration.

This procedure was repeated with various trained strains developed by continued subculture at one given drug concentration. Cells trained at one concentration were inoculated into a higher concentration to start a more highly trained strain. Usually about ten subcultures at a given level were sufficient to bring the training process to a limit but a larger number was given before the strain was tested. Each subculture represents 8—10 generations. In this

[1] Lodge and Hinshelwood, *J.*, 1939, 1692.
[2] Fogg and Lodge, *Trans. Faraday Soc.*, 1945, **41**, 359.
[3] Spray and Lodge, *ibid.*, 1943, **39**, 1.
[4] Phillips and Hinshelwood, *J.*, 1953, 3679.
[5] Lehninger, "Harvey Lectures," Academic Press, New York, 1954, Vol. 49, p. 176.
[6] Wild and Hinshelwood, *Proc. Roy. Soc.*, 1955, *B*, **144**, 287.

XUM

way the series of strains was developed for which the lag–concentration curves are plotted in Fig. 3.

The results show that a strain trained to a concentration m is resistant to all concentrations up to approximately $3m$. The resistance of a trained strain, as measured by the drug concentration required to produce a standard lag, is proportional to the "training concentration" (Fig. 4). The lag–concentration curves are shown for only four trained strains, corresponding to 300, 400, 500, and 700 mg./l. although two other strains trained to 1500 and 3000 mg./l. were maintained. Both these were found to be fully resistant, in the sense of showing no lag, to concentrations up to the solubility limit of about 5·6 g./l.

The resistance of some of the above strains was also tested by determining the fraction of the inoculum surviving when spread on a drug agar plate. Results showing the increased survival of the two trained strains are given in Table 2.

Measurements were also made of the times of appearance and the rates of development of colonies on drug plates.[7] A number of cells was plated such that between 50 and 200 of them finally gave rise to colonies. The fraction of cells of the untrained strain surviving to form colonies (α_∞) was about 10^{-5} at the concentration of drug used. For the trained strain it was unity, corresponding to 100% colony formation.

FIG. 3. *Lag–concentration curves for* Bact. lactis aerogenes *trained at various concentrations (m) of dinitrophenol. The values of m are shown above each curve (mg./l.).*

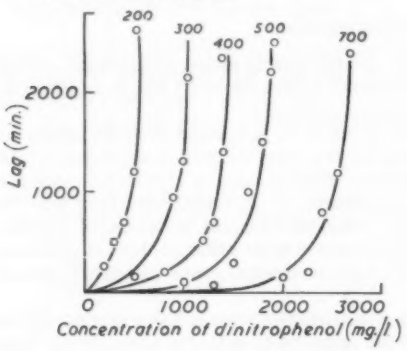


FIG. 4. *Concentrations of dinitrophenol giving lags of* 1200 *minutes for* Bact. lactis aerogenes *trained at various concentrations (m) of dinitrophenol.*

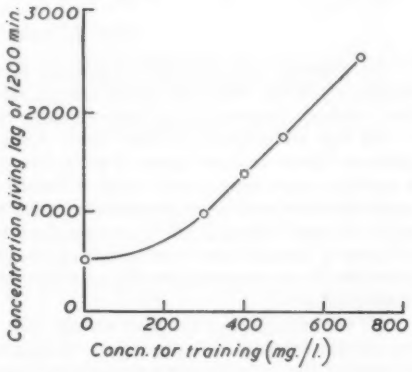


TABLE 2. *Survival on dinitrophenol–agar plates.*

Concn. of dinitrophenol in the agar (mg./l.)	Fraction surviving			Concn. of dinitrophenol in the agar (mg./l.)	Fraction surviving		
	Untrained strain	Strain trained at 400 mg./l.	Strain trained at 1500 mg./l.		Untrained strain	Strain trained at 400 mg./l.	Strain trained at 1500 mg./l.
0	1	1	1	750	3×10^{-6}	—	—
125	6×10^{-1}	1	1	1000	1×10^{-5}	6×10^{-1}	7×10^{-1}
250	4×10^{-2}	8×10^{-1}	1	2000	—	4×10^{-2}	3×10^{-1}
375	6×10^{-4}	—	—	3000	—	6×10^{-4}	2×10^{-1}
500	1×10^{-5}	9×10^{-1}	9×10^{-1}				

The time at which each colony on the plate became visible to the naked eye was recorded, and the sizes were then measured at intervals of 4—8 hours. The results were expressed as the fraction (α_t) of the inoculum which had appeared and the fraction which, by a time t from inoculation, had reached a standard size designated "large." Fig. 5 shows the increase with time both in the total number, T, and the number of "large" colonies, L, by plotting α_t/α_∞ against t.

The delay in the appearance of colonies from the untrained strain as compared with those from the trained strain is not due to the presence of a large excess of sensitive cells. Experiments in which a small number of trained cells were mixed with a large excess of sensitive cells

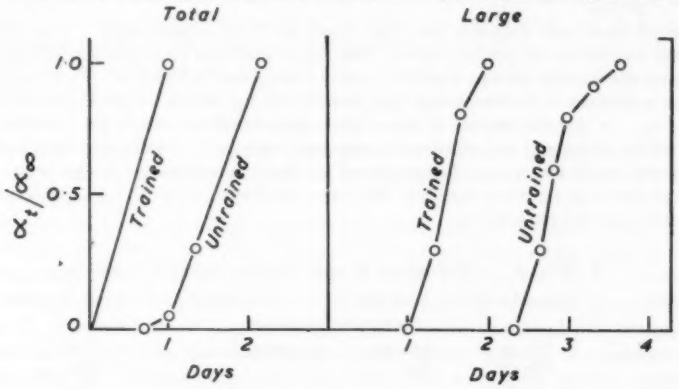
[7] Dean and Hinshelwood, *Proc. Roy. Soc.*, 1955, *B*, **144**, 297.

showed that the former developed into colonies at the same rate as when plated alone. In this experiment the fully trained cells were easily differentiated from the small fraction surviving from the untrained culture. They all formed colonies after one day, while the untrained cells did not do so until two or three days after inoculation. Large colonies were formed from trained cells in two days and from untrained in three or four days. These time relationships are in accordance with the results of the previous experiment in which the two types of cell were plated separately.

Various effects of prolonged cultivation of *Bact. lactis aerogenes* in the presence of high concentrations of dinitrophenol were also investigated. The strain used for these tests had been given more than 50 subcultures at 1500 mg./l. of the drug, and then showed no lag at concentrations up to the solubility limit.

Preliminary experiments showed that the simple biochemical tests normally used to define the organism were not affected by the training process. The trained strain was still able to ferment sucrose, lactose, and inositol, but not dulcitol, and it produced acetylmethylcarbinol (3-hydroxybutan-2-one) when grown in glucose.

FIG. 5. *Effect of training on growth of colonies on plates.* (*For explanation of symbols see text.*)



In view of the well-known specific action of dinitrophenol on the metabolism of cell extracts experiments were made to assess the respiratory and synthetic ability of dinitrophenol-trained cells. To test the respiratory activity of these cells they were spread on agar plates containing 2 : 3 : 5-triphenyltetrazolium chloride at 30 mg./l., this compound being applicable for the estimation of dehydrogenases, acting as hydrogen acceptor in place of oxygen and being reduced to a carmine-red formazan.[8] The colonies from the trained cells became coloured in the same time, and to the same intensity, as the colonies of control plates prepared with cells unexposed to the action of dinitrophenol. Moreover, when mixtures of the two types of cell were used as inocula the resulting colonies were not distinguishable. Cells having a permanent respiratory deficiency induced by exposure to the drug should have been detectable by such tests.

Another simple means of assessing the efficiency of the respiratory enzyme system consists in measuring the maximum population attainable in a medium containing a limiting amount of glucose, so that multiplication ceases on account of exhaustion of the food supply and the maximum population is linearly related to the concentration of the glucose. (The medium actually used contained one-fiftieth of the usual concentration.) Aerobic processes of oxidation make available much more energy for each unit of dissimilated carbohydrate than anaerobic mechanisms. Thus if normal aerobic mechanisms are impaired the glucose will be much less efficiently used and a much smaller population will be reached. The maximum populations, as measured by turbidity 24 hours after inoculation, are given in Table 3, which shows close

[8] Brodie and Gots, *Science*, 1951, **114**, 40; 1952, **116**, 588; Smith, *Science*, 1951, **113**, 753; Kun and Abood, *ibid.*, 1949, **109**, 144; Kun, *Proc. Soc. Expt. Biol. Med.*, 1951, **78**, 195; Lindemann, *Schweiz. Z. Allg. Pathol. Bakteriol.*, 1954, **17**, 311.

XUM

agreement between the results for trained and untrained cells. Even with the drug actually present in the limiting medium the population reached is not significantly less than normal.

In another series of experiments the rate of adaptation to new sources of carbon was examined. Measurements were made of the lags shown when the highly trained strain was given a first subculture in a medium containing various new carbon sources. The drug-trained

TABLE 3. *Glucose utilisation (total cell mass per ml. after exhaustion of glucose) by normal and trained strains.*

Strain	Drug concn. (mg./l.)	Turbidity reading	Equiv. population in 10^6/ml.	Drug concn. (mg./l.)	Turbidity reading	Equiv. population in 10^6/ml.
Trained to 1500 mg./l.	0	1·33	92	500	1·35	88
		1·32	94		1·36	86
					1·34	90
Control	0	1·32	94	0	1·32	94

strain and a normal strain as control were grown in a limiting glucose medium until all the glucose was exhausted and then inoculated into the new medium so as to give an initial count of about 1×10^6/ml.

A strain of *Bact. coli mutabile* was also used in these experiments. The dinitrophenol-trained strain was given 20 subcultures at 1500 mg./l. and was resistant to the solubility limit.

The lags of the trained strains and the controls are given in Table 4. In each case training to high concentrations of dinitrophenol lengthened the lag shown in the new carbon substrate by about 50%. A parallel series of tubes were inoculated in which the medium contained 500 mg./l. of dinitrophenol in addition to the new substrate. Although the trained strains were completely resistant to the dinitrophenol at this concentration in the sense of showing no lag in its presence in a glucose medium, they were unable to undergo the adaptation necessary to grow in the new carbon sources.

TABLE 4. *Adaptation to new carbon sources (time lag).*

Substrate	Trained strain	Control	Substrate	Trained strain	Control
		Bact. lactis aerogenes			
Acetate	700 min.	480 min.	D-Arabinose	230 hr.	160 hr.
	750 ,,	560 ,,		254 ,,	162 ,,
				246 ,,	169 ,,
				220 ,,	142 ,,
		Bact. coli mutabile			
Succinate	480 min.	310 min.	Lactose	144 hr.	96 hr.
	500 ,,	340 ,,		150 ,,	98 ,,

DISCUSSION

The actions of the two inhibitors studied present a sharp contrast with one another. Dinitrophenol shows a familiar pattern of behaviour such as is shown with proflavine and other compounds, namely, the production of a lag when the cells are first subcultured into the drug medium and its rapid elimination in successive subcultures. Striking differences in the action of disodium dihydrogen ethylenediamine-*NNN'N'*-tetra-acetate are its failure, at any concentration, to give rise to a lag, and the wide range of concentrations over which it may be used without completely inhibiting growth.

Quantitative interpretation of the results obtained for the latter inhibitor is difficult, first because the presence in the medium of Mg^{++} ions with which the inhibitor forms a complex makes the concentration of both uncertain and, secondly, because the results obtained relate to the mean generation time which is a more complex property than the lag and is determined by all the interdependent processes connected with metabolism and synthesis.

There are, however, two mechanisms which would account naturally for the training processes outlined above: (1) Certain enzyme systems require specific trace cations as

activators. By complex formation with such traces the drug could reduce the activity of the enzyme. (2) The drug is specifically adsorbed on one or more enzymes and reduces their activity. In either of these eventualities the cells might develop, to a limited extent, alternative pathways of metabolism in which the inhibited enzyme is unnecessary. The adoption of the new pathway and its development to a state of maximum efficiency would be manifested as a gradually increasing growth rate, the limiting mean generation time indicating the attainment of the state of maximum efficiency for the new pathway. Alternatively, adaptation might take place by expansion of the enzyme or enzymes affected so as to compensate the reduced activity. Again a gradual increase in growth rate would be expected.

The training to dinitrophenol may be considered in the light of two usual alternatives: selection within an initially heterogeneous population, or induced changes in individual cells. The lag–concentration curves show that a number of stable strains can be obtained differing in degree of resistance, this degree being simply related to the training concentration. There is the usual difficulty in constructing a plausible hypothesis attributing these separate strains, each with definite limits of resistance, to the selection of initially resistant cells. Unless a surprising range of mutations is postulated and thus an indefinite number of distinct types of pre-existing resistant cells, growth in any inhibitory concentration should lead to a strain immune to all concentrations. It is difficult to imagine that training in 300 mg./l. should select out pre-existing types resistant to 1100 mg./l. whilst training in 400 mg./l. selects a different type resistant up to 1900 mg./l.

The experimental results are more in accordance with the mechanism in which exposure of the culture to the drug causes a response in the majority rather than in a very small proportion of the cells.

The difference in the time of appearance of colonies on drug plates when trained and untrained strains are plated is very significant. The extra 28 hours taken for the formation of 100% of colonies from the untrained strain must, it would seem, be due to the gradual adaptation taking place on the plate, the retardation having been shown not to be due to the presence of a large excess of sensitive cells. Thus even the small proportion surviving from the untrained inoculum are quantitatively not of the type in the trained inoculum.

The lags observed during adaptation to new carbon sources of the dinitrophenol-trained strain show two interesting features. First, they are increased by about 50% as compared with those of a normal strain, and this fact suggests a modification of some of the biochemical properties of the cells by the training. If the adaptive processes involve a change in the balance of the various enzyme systems it is perhaps to be expected that changes also will occur in the adaptive potentialities of the cells. Secondly, in no case would the trained strain become adapted to the new carbon source in presence of the drug even at a concentration well below that to which the cells were resistant. Dinitrophenol inhibits enzymic adaptation in normal unadapted bacteria through the prevention of synthesis, but the trained strain fails to become adapted although, as was shown by various simple tests, the normal synthetic processes appear to function even in the presence of the drug. Particularly in cases where the lag period is a long one, as in the adaptation to D-arabinose, it may be the long-term protein-precipitating properties which are operative rather than the specific action to which the cells are apparently resistant. During a prolonged lag considerable slow degeneration of the cell could take place, though it must remain a possibility that the drug inhibits the formation of adaptive enzymes even while normal enzymes still function.

PHYSICAL CHEMISTRY LABORATORY, OXFORD. [*Received, February 12th*, 1958.]

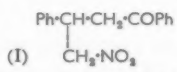
XUM

460. *Chalcones and Related Compounds. Part V.* Addition of Nitro-compounds to Chalcones.*

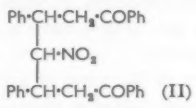
By W. Davey and D. J. Tivey.

Addition of nitromethane and nitroethane to chalcones is best catalysed by sodium methoxide; diethylamine is less effective. Diethylamine is the preferred catalyst for addition of nitroacetic ester to chalcone. In some cases two isomeric adducts were formed and separated; these adducts of diaryl-pyrrolines and -pyrrolidines have been reduced and the structures of the products studied. Reduction of the adducts to yield other products was less effective.

As a result of extensive studies Kohler *et al.*[1] have recommended sodium methoxide as condensing agent for the addition of nitromethane and nitroethane to chalcones and the use of excess nitroalkane to avoid side-reaction. The primary addition product of chalcone and nitromethane is 4-nitro-1 : 3-diphenylbutan-1-one (I), further reaction yielding the bis-adduct (II). Kloetzel[2] advised the use of diethylamine as catalyst and a 10 : 1 nitromethane : chalcone ratio to avoid formation of the product (II). Rogers[3] has also added nitromethane to substituted chalcones. Sodium methoxide has been found by us to be the most effective catalyst for a number of new additions of nitromethane to chalcones and only in the case of chalcone was there any tendency for further reaction to occur. With



(I)



(II)

diethylamine as catalyst reaction was far less complete but again no tendency to form bis-adducts was observed. Previous workers[1,3] have found difficulty in obtaining these adducts crystalline; in our hands extraction of the oils with benzene and removal of the benzene by distillation has given solid adducts, probably by completely drying them. Fishman and Zuffanti[4] claimed the use of calcium hydride for such additions but this reagent gave incomplete addition of nitromethane to chalcone. Kloetzel[2a] and Kohler *et al.*,[1] on adding nitroethane to chalcone, isolated two geometrically isomeric, racemic adducts. In our work nitroethane was added to five substituted chalcones, with sodium methoxide as catalyst, and in three cases pairs of solid isomers were separated. Diethylamine or ammonia as catalyst gave incomplete reaction.

Although Dornow and Frese[5] added nitroacetic ester to benzylideneacetone in presence of diethylamine no reference to such addition to chalcone has been found. We found that sodium ethoxide or hydroxide failed to effect the addition to chalcone but use of diethylamine was effective. A crude adduct was obtained from 4 : 4′-dimethoxychalcone but in other cases no success was achieved. Alkaline hydrolysis of the adduct of nitroacetic ester and chalcone gave the ketone (I), decarboxylation occurring.

Reduction of the nitro-ketone adducts and their conversion into 2 : 4-diaryl-pyrrolines and -pyrrolidines has also been studied. Kohler and Drake[1] obtained a mixture on hydrogenation of the adduct (I), and Sonn[6] obtained pyrrolines by use of iron and acetic or

* Part IV, *J.*, 1958, 1230.

[1] Kohler, *J. Amer. Chem. Soc.*, 1916, **38**, 889; Kohler and Drake, *ibid.*, 1923, **45**, 2144; Kohler and Williams, *ibid.*, 1919, **41**, 1644; Kohler and Rao, *ibid.*, 1919, **41**, 1697; Kohler and Smith, *ibid.*, 1922, **44**, 624; Kohler, *ibid.*, 1924, **46**, 503.

[2] (*a*) Kloetzel, *J. Amer. Chem. Soc.*, 1947, **69**, 2271; (*b*) Kloetzel, Pinkus, and Washburn, *ibid.*, 1957, **79**, 4222.

[3] Rogers, *J.*, 1943, 590.

[4] Fishman and Zuffanti, *J. Amer. Chem. Soc.*, 1951, **73**, 4466.

[5] Dornow and Frese, *Annalen*, 1952, **578**, 122.

[6] Sonn, *Ber.*, 1935, **68**, 148.

hydrochloric acid. Kloetzel [2a] obtained pyrrolines by hydrogenation over Raney nickel at 25° but later, with Pinkus and Washburn,[2b] converted the adduct (I) into 2 : 4-diphenylpyrrolidine with freshly prepared Raney nickel. We reduced the adducts with zinc and acetic acid at 40—60° to the pyrrolines, but excess of zinc and careful temperature control were necessary to obtain good yields. Although Putckhin [7] claimed hydrogenation of pyrroles to pyrrolidines in presence of palladium oxide, it has been found that hydrogenation of our adduct (I) in ethanol with a palladium–charcoal catalyst gave 2 : 4-diphenylpyrroline in good yield, and this method offers advantages in ease of reaction, lack of necessity for careful control of temperature, ease of isolation, and purity of product; excess of zinc was maintained throughout in the chemical reduction and, since all the pyrrolines were difficult to crystallise, purification *via* the picrate was employed.

Reduction of the two isomeric 1 : 3-diaryl-4-nitropentan-1-ones by chemical or catalytic methods gave two isomeric pyrrolines, but there is no evidence of their configurations. Hydrogenation of ethyl 3 : 5-diphenyl-2-nitro-5-oxopentanoate in ethanol with palladium–charcoal also gave the pyrroline ester.

Reduction of the 2 : 4-diarylpyrrolines to the pyrrolidines was effected in ethanol in presence of freshly prepared Raney nickel W.7, hydrogenation being stopped when the requisite hydrogen uptake had occurred. Further hydrogenation occurred but at about one fifth of the initial rate. Hydrogenation of the isomeric pyrrolines gave isomeric pyrrolidines; 2-ethoxy-3 : 5-diphenylpyrrolidine was obtained by hydrogenation of the pyrroline ester.

Some further reductions were carried out on the nitro-ketone adducts. Reduction of 4-nitro-1 : 3-diphenylbutan-1-one to the alcohol by aluminium *iso*propoxide or, better, sodium borohydride, gave a product, presumably a mixture of two isomers, from which one was obtained solid. Hydrogenation of the solid isomer gave a solid 4-amino-1 : 3-diphenylbutan-1-ol. Reduction of the nitro-ketone by potassium borohydride and hydrogenation of the crude product gave the same solid amino-alcohol and an oily isomer. Zinc and acetic acid yielded one isomer of 4-acetamido-1 : 3-diphenylbutan-1-ol, identical with the acetylation product of the above solid amine. Sodium borohydride reduced ethyl 2-nitro-5-oxo-3 : 5-diphenylpentanoate in aqueous ethanol to 4-nitro-1 : 3-diphenylbutan-1-ol, decarboxylation having occurred after hydrolysis during the reduction, and the product was purer than that obtained by borohydride reduction of the nitro-ketone, the ester group having perhaps made reduction more stereospecific. Reduction of the ester by aluminium *iso*propoxide and of other nitro-ketones by borohydride gave oils, or in some cases unchanged starting materials.

Some study has been made of the structures of the pyrrolines and pyrrolidines prepared in this work. Reduction of a 2-substituted pyrrole can give five possible pyrrolines. Although many pyrrolines have been reported their structures have often not been uncertain. Δ^3-Pyrrolines are produced on the reduction of pyrroles with zinc and acid [8] unless aromatic substituents are present,[9] the structures having been established by ozonolysis,[10] reaction with bromine or permanganate, formation of an *N*-benzoyl derivative, an infrared absorption band at 3·02 μ (assigned to the NH group), and a study of quaternary pyrrolidinium salts.[11] For Δ^1- and Δ^2-pyrrolines the evidence is less reliable and some earlier references to Δ^1-compounds probably refer to Δ^2-isomers and *vice versa*; evidence of structure has been obtained from studies of reactivity towards ozone, bromine, permanganate, benzoyl chloride, and methylmagnesium iodide [11] and by infrared spectra. Acid

[7] Putckhin, *J. Russ. Phys. Chem. Soc.*, 1930, **62**, 2216.
[8] Anderlini, *Ber.*, 1889, **22**, 2512; Knorr and Rabe, *Ber.*, 1901, **34**, 3497; Ciamician, *ibid.*, p. 3952; Langheld, *Ber.*, 1909, **42**, 2373.
[9] Gitsels and Wibaut, *Rec. Trav. chim.*, 1941, **60**, 50; Dhent and Wibaut, *ibid.*, 1944, **63**, 81; Sonn, *Ber.*, 1935, **68**, 148; 1939, **72**, 2150.
[10] Treibe and Dinelli, *Annalen*, 1935, **517**, 170; Blaise, *Compt. rend.*, 1914, **158**, 1686; Blaise and Cornillot, *ibid.*, 1924, **178**, 1617.
[11] Lukes and Preucil, *Coll. Czech. Chem. Comm.*, 1938, **10**, 384.

XUM

reduction of arylpyrroles and cyclisation methods [12] give Δ^1- or Δ^2-pyrrolines. *cis*- and *trans*-Isomers of substituted pyrrolines and pyrrolidines [13] have been isolated.[11,12] For 2 : 4-diphenylpyrroline Kloetzel, Pinkus, and Washburn [2b] found no infrared band in the NH region although the general level of absorption was high in the region 2·5—3·5 μ; they pointed out the difficulties of infrared spectral studies in the NH region for pyrrolines and pyrrolidines and that the intensity of absorption depends upon the nature of substituents in the vicinity of the nitrogen atom and upon the medium. They stated however that their results are in harmony with a Δ^1-structure The infrared spectra of our 2 : 4-diarylpyrrolines suggested the possibility of Δ^2-structures, since a band at 3100—3400 cm.$^{-1}$ (Nujol mull) indicated a possible NH group.[14] Two aromatic bands at 1607 and 1500 cm.$^{-1}$ were also present in the 2 : 4-diphenylpyrroline spectrum. Although reduction of the 2 : 4-diarylpyrrolines could give *cis*- and *trans*-pyrrolidines, only one form was obtained in good yield The spectra of the isomers of 5-methyl-2 : 4-diphenylpyrroline contained very weak bands at about 3300 cm.$^{-1}$, suggesting possible tautomerism between Δ^1- and Δ^2-structures; absence of a band at 3300 cm.$^{-1}$ in the case of 5-ethoxycarbonyl-2 : 4-diphenylpyrroline suggested a Δ^1-structure, an ester-carbonyl band at 1738 and aromatic bands at 1615 and 1495 cm.$^{-1}$ also being present in this spectrum. Aromatic bands at 1607 and 1497 cm.$^{-1}$ were also present in the spectra of the isomeric 5-methyl-2 : 4-diphenylpyrrolines, and the former may have masked any band due to a C=N group at 1590 cm.$^{-1}$.

Experimental

Addition of Nitromethane to Chalcones.—(*a*) *By Kohler's method.*[1] Addition of sodium (15 g.) in methanol (175 ml.) to a stirred solution of chalcone (104 g.) and nitromethane (37·5 g.) in methanol (175 ml.) at 40° gave, on cooling and acidification, a product which crystallised from ethanol in colourless needles (114 g., 85%) of 1 : 3-diphenyl-4-nitrobutan-1-one, m. p. 101—102° (Kohler gives m. p. 103°). (*b*) *Diethylamine method.* Chalcone (20·8 g., 0·1 mole), nitromethane (60 g., 1·0 mole), and diethylamine (8 g., 0·1 mole) in methanol (70 ml.) were set aside at room temperature for 7 days. Acidification with dilute acetic acid and addition of water (50 ml.) gave a viscous oil which was extracted with benzene (150 ml.). Water-washing and evaporation of the benzene layer *in vacuo*, and recrystallisation from ethanol gave 1 : 3-diphenyl-4-nitrobutan-1-one (19·4 g., 72%).

3-*p*-Methoxyphenyl-4-nitro-1-phenylbutan-1-one, prepared by method (*a*), but at 50° for 30 min., in 61% yield, had m. p. 63—65° (decomp.) (Rogers [3] gives m. p. 66°, with previous sintering and does not state a yield).

1 : 3-*Di*-p-*methoxyphenyl*-4-*nitrobutan*-1-*one* was obtained by method (*a*) as needles, m. p. 75° (70%) (Found: C, 65·1; H, 5·6; N, 4·1. $C_{18}H_{19}O_5N$ requires C, 65·6; H, 5·8; N, 4·2%) (Rogers [3] describes this as an oil).

3-p-*Methoxyphenyl*-4-*nitro*-1-p-*tolylbutan*-1-*one* was obtained by method (*a*) as an oil which on benzene-extraction, removal of the benzene *in vacuo*, and keeping the product under light petroleum (b. p. 60—80°), formed needles, m. p. 54—56° (64·1%) (Found: C, 69·3; H, 6·0; N, 4·7. $C_{18}H_{19}O_4N$ requires C, 69·0; H, 6·1; N, 4·5%).

1-m-*Hydroxyphenyl*-4-*nitro*-3-*phenylbutan*-1-*one*, obtained by method (*a*) at 50° for 1 hr., formed needles (from benzene), m. p. 98—99° (70·4%) (Found: C, 67·8; H, 5·2; N, 5·2. $C_{16}H_{15}O_4N$ requires C, 67·4; H, 5·3; N, 4·9%).

3-m-*Hydroxyphenyl*-1-p-*methoxyphenyl*-4-*nitrobutan*-1-*one*, obtained by method (*a*) but at the b. p. for 30 min., formed needles [from benzene–light petroleum (b. p. 60—80°)], m. p. 107—108° (95·5%) (Found: C, 70·1; H, 5·2; N, 4·1. $C_{17}H_{17}O_5N$ requires C, 64·8; H, 5·4; N, 4·4%).

3-o-*Chlorophenyl*-1-p-*tolyl*-4-*nitrobutan*-1-*one*, obtained by method (*a*) at 40° (addition) and then 50° (30 min.), formed needles [from light petroleum (b. p. 60—80°)], m. p. 80° (59%) (Found: C, 64·0; H, 5·1; N, 4·8. $C_{17}H_{16}O_3NCl$ requires C, 64·3; H, 5·0; N, 4·4%).

[12] Roberts and Ross, *J.*, 1952, 4288.
[13] Evans, *J. Amer. Chem. Soc.*, 1951, **73**, 5230.
[14] Bellamy, "Infra-red Spectra of Complex Molecules," Methuen, London, 1954, p. 213; Barnes *et al.*, "Infra-red Spectroscopy," Rheinhold Publ. Corp., New York, p. 19.

Additions of Nitroethane to Chalcones.—Method (*a*) above was modified: To a stirred solution of chalcone (18·6 g., 0·09 mole) and nitroethane (8·2 g., 0·11 mole) in methanol (40 ml.) at 50° was added rapidly a solution from sodium (2·8 g.) in methanol (30 ml.). After 1 hr. at 50°, the mixture was cooled and acidified with dilute acetic acid and after 12 hr. the crude product was taken up in benzene (150 ml.), and the benzene extract dried (Na_2SO_4) and evaporated to give a product, m. p. 47—60° (23·9 g.). This product was dissolved in boiling ether (100 ml.) and crystals deposited after 1 hour's cooling were filtered off (10 g.; m. p. 80°). Concentration of the filtrate to 65 ml. and cooling gave a second crop, m. p. 75° (2 g.), and evaporation of the filtrate gave a product m. p. 55° (9 g.). The two high-melting fractions were combined and twice recrystallised from ether, to give needles of 4-nitro-1 : 3-diphenylpentan-1-one A, m. p. 100° (5·2 g., 20%); recrystallisation from ether of the low-melting form gave the other isomer B as needles, m. p. 67° (3·5 g., 14%) (Kohler [1] gives m. p.s 100° and 72°).

4-*Nitro*-1-*phenyl*-3-p-*tolylpentan*-1-*one* was prepared as above, as needles A (from methanol), m. p. 115—116° (48%) (Found: C, 72·5; H, 6·2; N, 4·4. $C_{18}H_{19}O_3N$ requires C, 72·7; H, 6·4; N, 4·7%), and crystals B (from methanol), m. p. 93—94° (15%) (Found: C, 72·4; H, 6·5; N, 4·8%).

1 : 3-*Di*-p-*tolyl*-4-*nitropentan*-1-*one* was obtained in the one form only, plates, m. p. 75° (60%) (Found: C, 73·6; H, 7·0; N, 4·6. $C_{19}H_{21}O_3N$ requires C, 73·3; H, 6·8; N, 4·5%).

3-p-*Methoxyphenyl*-4-*nitro*-1-*phenylpentan*-1-*one* was obtained as needles A, m. p. 111—112° (32%) (Found: C, 68·7; H, 6·2; N, 4·4. $C_{18}H_{19}O_4N$ requires C, 69·0; H, 6·1; N, 4·5%), and as needles B (from ether), m. p. 84—85° (25%) (Found: C, 69·1; H, 6·2; N, 4·5%).

1 : 3-*Di*-p-*methoxyphenyl*-4-*nitropentan*-1-*one* was obtained in one form only, needles (from benzene), m. p. 95° (60%) (Found: C, 66·0; H, 6·0; N, 4·0. $C_{19}H_{21}O_5N$ requires C, 66·5; H, 6·1; N, 4·1%).

Addition of Ethyl Nitroacetate to Chalcones.—Ethyl nitroacetate was prepared by the following modified Bouveault and Wahl's method: Ethyl acetoacetate (5 g.), mixed with acetic anhydride (25 g.), was stirred during addition of a mixture of nitric acid (27 g.; *d* 1·52) and acetic anhydride (27 g.), the temperature being kept at 32—34°. Then the mixture was poured into water and the oil extracted with benzene (2 × 50 ml.). The benzene extract was washed with water and evaporated under reduced pressure and the oily residue distilled, to give ethyl nitroacetate (1·5 g., 27%), b. p. 93—96°/9 mm., n_D^{20} 1·1992. The extraction procedure used by Bouveault *et al.*[15] was unnecessary and gave no higher yield than distillation of the product. Other methods [16] were less convenient in spite of giving higher yields.

Ethyl 2-*Nitro*-5-*oxo*-3 : 5-*diphenylpentanoate.*—Chalcone (8·9 g., 0·045 mole) in ethanol (50 ml.) was treated with ethyl nitroacetate (6·3 g., 0·047 mole) and diethylamine (0·3 ml.) under reflux for 15 min., cooled, acidified with 50% acetic acid (5 ml.), and diluted with water (20 ml.); the ester which separated solidified and recrystallised from ethanol as needles, m. p. 128—129° (11 g., 94%) (Found: C, 67·2; H, 5·8; N, 4·1. $C_{18}H_{19}O_5N$ requires C, 66·9; H, 5·6; N, 4·1%). Use of sodium methoxide as catalyst failed to achieve reaction, the sodium salt of ethyl nitroacetate being precipitated.

Hydrolysis. The nitro-ester (1 g.,) was refluxed with ethanol (5 ml.) and 2N-sodium hydroxide (3 ml.) for 1 hr., then filtered from precipitated sodium carbonate (0·25 g.) and acidified with 2N-hydrochloric acid to give an oil, which crystallised from ethanol to give colourless needles of 4-nitro-1 : 3-diphenylbutan-1-one, m. p. and mixed m. p. 98° (0·6 g., 74%) (Found: C, 71·5; H, 5·8. $C_{16}H_{15}O_3N$ requires C, 71·4; H, 5·6%).

Addition of nitroacetic ester (5·3 g., 0·04 mole) to 4 : 4′-dimethoxychalcone (10 g., 0·037 mole) in ethanol (50 ml.) and diethylamine (3 ml.) under reflux for 2 hr. gave an oil (4·9 g.). This (2 g.) in ethanol (5 ml.) with 2 : 4-dinitrophenylhydrazine (1·5 g.) in sulphuric acid (2 ml.; *d* 1·84) and ethanol (20 ml.) gave red needles of *ethyl* 3 : 5-*di*-(p-*methoxyphenyl*)-2-*nitro*-5-*oxopentanoate* 2 : 4-*dinitrophenylhydrazone*, m. p. 97—99° (0·5 g.) (Found: C, 54·4; H, 4·3; N, 12·6. $C_{27}H_{27}O_{10}N_5$ requires C, 55·7; H, 4·7; N, 12·0%).

4-*Nitro*-1 : 3-*diphenylbutan*-1-*ol.*—(*a*) Reduction of 4-nitro-1 : 3-diphenylbutan-1-one (8 g., 0·03 mole) by aluminium *iso*propoxide (8·1 g., 0·04 mol.) and toluene (50 ml.) under a Fenske column (3″) gave acetone (3 ml. Calc., 1·7 g.) and a product which, on acidification with 2N-sulphuric acid (60 ml.), extraction with ethyl acetate, and evaporation of the extract gave

[15] Bouveault and Wahl, *Bull. Soc. chim. France*, 1904, **31**, 847.
[16] Steinkopf, *Annalen*, 1923, **434**, 21; Fever, Weisblat, and Lyttle, *J. Amer. Chem. Soc.*, 1949, **71**, 3079.

XUM

an oil; this partly solidified after two weeks and, recrystallised from light petroleum (b. p. 40—60°), gave **4-*nitro*-1 : 3-*diphenylbutan*-1-*ol*** (2·2 g.) as needles, m. p. 77—79° (Found: C, 70·5; H, 6·1; N, 5·1. $C_{16}H_{17}O_3N$ requires C, 70·8; H, 6·3; N, 5·2%).

(*b*) 4-Nitro-1 : 3-diphenylbutan-1-one (5 g., 0·019 mole) in ethanol (40 ml.) was slowly added to a solution of potassium borohydride [1·5 g. in water (2 ml.) and ethanol (50 ml.)] at room temperature with stirring and set aside for 12 hr. Removal of most of the ethanol *in vacuo* and addition of 2N-hydrochloric acid (20 ml.) gave a syrup, which was extracted with benzene. Removal of the benzene gave an oil which partially solidified after 2 weeks and on recrystallisation from light petroleum (b. p. 40—60°) gave 4-nitro-1 : 3-diphenylbutan-1-ol, needles, m. p. 77—79° (2 g., 40%) (Found: C, 70·6; H, 6·4; N, 5·2%).

4-*Amino*-1 : 3-*diphenylbutan*-1-*ol*.—(*a*) The nitro-alcohol (4 g.) in ethanol (30 ml.) was hydrogenated in presence of 5% palladium–charcoal (0·5 g.) until the requisite hydrogen uptake had taken place. Filtration, removal of ethanol *in vacuo*, and crystallisation from benzene gave **4-*amino*-1 : 3-*diphenylbutan*-1-*ol*** as needles, m. p. 121—122° (2·9 g., 85%) (Found: C, 79·8; H, 7·9; N, 5·6. $C_{16}H_{19}ON$ requires C, 79·6; H, 7·9; N, 5·8%).

(*b*) The nitro-ketone (10 g., 0·037 mole) in ethanol (200 ml.) was treated with potassium borohydride solution (25 g., 0·043 mol.) in 3 : 17 aqueous ethanol (55 ml.) at 30° for 1½ hr., then evaporated *in vacuo* to a viscous syrup. Addition of 2N-hydrochloric acid (30 ml.) and benzene-extraction, followed by removal of solvent, gave an oil (8 g.). Hydrogenation of this oil in ethanol with a 70% palladium–charcoal catalyst (1·0 g.) led to absorption of 2·85 mols. Filtration and evaporation gave an oil from which 4-amino-1 : 3-diphenylbutan-1-ol was obtained as needles, m. p. 120—121° (3 g., 33%). Although no crystalline isomer could be isolated from the mother-liquors, the oil (4·2 g.) obtained after removal of solvent was treated in ether (20 ml.) with picric acid (4·2 g.) in ether (100 ml.), to give a yellow precipitate (8 g.; m. p. 165—170°) which, recrystallised from ethanol, gave a *picrate* as needles, m. p. 169—170° (6·0 g.) (Found: C, 56·3; H, 4·8; N, 11·7. $C_{22}H_{22}O_8N_4$ requires C, 56·2; H, 4·7; N, 11·9%). Treatment of this picrate (2 g.) with 2N-alkali (20 ml.), extraction with benzene (20 ml.), and removal of the benzene *in vacuo* gave the low-melting *isomer* as an oil (Found: C, 79·3; H, 7·8; N, 5·5. $C_{16}H_{19}ON$ requires C, 79·6; H, 7·9; N, 5·8%).

4-*Acetamido*-1 : 3-*diphenylbutan*-1-*ol*.—4-Nitro-1 : 3-diphenylbutan-1-one (9·3 g., 0·034 mole) in ethanol (100 ml.) was added slowly with stirring to potassium borohydride (4·7 g., 0·087 mole) in 95% ethanol (250 ml.) and kept at room temperature for 12 hr., then most of the ethanol was removed *in vacuo*. Acidification with 2N-hydrochloric acid gave a viscous oil which was extracted with benzene. From the benzene extract an oil (9 g.) was isolated which was dissolved in glacial acetic acid (30 ml.) at 50°, stirred, and reduced at 50° with zinc dust (15 g.). The mixture was kept at 50° for a further 15 min., cooled, and filtered, the residue being washed with a little acetic acid. The filtrates were basified with 5N-sodium hydroxide and extracted with benzene (2 × 100 ml.). After washing and removal of the benzene *in vacuo* the resulting syrup (7 g.) was dissolved in benzene (25 ml.) and set aside; crystals (4 g.) were obtained. Recrystallisation from ethanol gave the *acetamide* as needles, m. p. 185° (3 g., 35%) (Found: C, 76·4; H, 7·6; N, 4·6. $C_{18}H_{21}O_2N$ requires C, 76·3; H, 7·5; N, 4·9%). The isomeric reduction product could not be isolated. Acetylation of the form, m. p. 121—122°, of the amine with boiling acetic acid for 1 hr. gave a product, which on purification *via* solution in benzene and recrystallisation from ethanol, furnished needles of the acetamide, m. p. and mixed m. p. 185°.

Reduction of Ethyl **2-*Nitro*-5-*oxo*-3 : 5-*diphenylpentanoate*.**—A solution of the ester (5 g.) in ethanol (100 ml.) was added rapidly to one of sodium borohydride (2·5 g.) in 85% ethanol (150 ml.) and kept for 12 hr. at room temperature. Evaporation *in vacuo*, acidification with 2N-acid (20 ml.), and benzene-extraction, yielded a syrup on removal of the benzene. This crystallised slowly on treatment with ethanol (10 ml.) and recrystallisation from light petroleum (b. p. 40—60°) gave needles of 4-nitro-1 : 3-diphenylbutan-1-ol (3 g., 75%), m. p. and mixed m. p. 79—80° (Found: C, 70·6; H, 6·4; N, 5·0. Calc. for $C_{16}H_{17}O_3N$: C, 70·8; H, 6·3; N, 5·2%). Attempts to reduce the ester with sodium borohydride at pH *ca.* 5·0, to avoid hydrolysis of the ester, or with aluminium *iso*propoxide in toluene, gave only the starting ester.

Preparation of **2 : 4-*Diarylpyrrolines*.**—(a) *By catalytic hydrogenation.* 4-Nitro-1 : 3-diphenylbutan-1-one (21·5 g., 0·056 mole) was hydrogenated in methanol (70 ml.) in presence of 10% palladium–charcoal (0·3 g.) in 30 min.; absorption then ceased, 0·17 mol. of hydrogen having been absorbed. Filtration and evaporation *in vacuo* to dryness gave a product (11·5 g.)

XUM

which was fractionated under reduced pressure to give an oil (b. p. 138—140°/0·5 mm.) which crystallised from light petroleum in needles (9·2 g., 75%), m. p. 49—50° (Rupe and Gisiger [17] give m. p. 50°).

(b) *With zinc dust and acetic acid.* 4-Nitro-1 : 3-diphenylbutan-1-one (15 g.) in glacial acetic acid (150 ml.) was reduced at 50—60° by the addition of zinc dust (50 g.) in 30 min. After a further 15 min. at 60°, the product was cooled and filtered, the residue being washed with acetic acid (2 × 20 ml.), poured into water (500 ml.) and basified with 5N-sodium hydroxide. The separated oil was extracted with benzene and recovered (10·2 g.). One half was distilled and recrystallised from light petroleum (b. p. 40—60°), to yield needles of 2 : 4-diphenylpyrroline, m. p. 48—50° (3·9 g., 58%). To the other portion, dissolved in ether (20 ml.), picric acid (4·2 g.) in ether (30 ml.) was added. The precipitate was filtered off and recrystallised from benzene to give 2 : 4-diphenylpyrroline picrate as yellow needles, m. p. 155—156° (Rupe and Gisiger [17] give m. p. 156°) (6·0 g.). The picrate was shaken with benzene (20 ml.), and 2N-sodium hydroxide (20 ml.) added; the organic layer was separated, washed with water, dried (Na_2SO_4), and evaporated *in vacuo*. Recrystallisation from light petroleum (b. p. 40—60°) gave needles of 2 : 4-diphenylpyrroline (2 g., 28%), m. p. 48—50° (total yield, 82%).

(c) *With zinc dust, acetic acid, and acetic anhydride.* 4-Nitro-1 : 3-diphenylbutan-1-one (10 g.) in acetic acid (50 ml.) and acetic anhydride (25 ml.) was reduced at 30—40° by zinc dust (40 g. in small portions) in 30 min. After a further hour at this temperature, the mixture was cooled and filtered, and the residue washed with acetic acid (2 × 10 ml.). The filtrate was poured into water (200 ml.) and made alkaline with 5N-sodium hydroxide. The separated oil (9·2 g.) was refluxed for 1½ hr. with 5N-hydrochloric acid (37 ml.) and ethanol (50 ml.). Evaporation gave an oil which yielded 2 : 4-diphenylpyrroline picrate (1·7 g.), m. p. 154—156°.

The following pyrrolines were obtained by method (b):

4-*p*-Methoxyphenyl-2-phenylpyrroline, needles [from light petroleum (b. p. 40—60°)], m. p. 26° (62%) (Rogers [3] gives m. p. 27°).

2 : 4-*Di*-p-*methoxyphenylpyrroline*, needles, m. p. 102° (70%) (Found: C, 76·4; H, 6·7; N, 4·7. $C_{18}H_{19}O_2N$ requires C, 76·8; H, 6·8; N, 5·0%); *picrate*, needles (from ethanol), m. p. 158—159° (Found: C, 56·2; H, 4·2; N, 10·7. $C_{24}H_{22}O_9N_4$ requires C, 56·3; H, 4·3; N, 11·0%).

2-m-*Hydroxyphenyl*-4-*phenylpyrroline*, plates, m. p. 118—120° (64%) (Found: C, 80·7; H, 6·8; N, 6·1. $C_{16}H_{15}ON$ requires C, 81·0; H, 6·3; N, 5·9%).

4-*m*-Hydroxyphenyl-2-*p*-methoxyphenylpyrroline (75%), b. p. 225—228°/0·6 mm.; *picrate*, needles (from ethanol), m. p. 145—146° (Found: C, 55·5; H, 4·3; N, 11·2. $C_{23}H_{20}O_9N_4$ requires C, 55·6; H, 4·0; N, 11·3%).

4-o-*Chlorophenyl*-2-p-*tolylpyrroline*, needles [from benzene–light petroleum (b. p. 60—80°)], m. p. 61—62° (76%) (Found: C, 75·4; H, 6·1; N, 5·5. $C_{17}H_{16}NCl$ requires C, 75·7; H, 5·9; N, 5·2%).

4-p-*Methoxyphenyl*-2-p-*tolylpyrroline*, b. p. 230—234°/0·5 mm. (85%) (Found: C, 81·2; H, 7·1; N, 5·6. $C_{18}H_{19}ON$ requires C, 81·5; H, 7·2; N, 5·3%); *picrate*, needles (from ethanol), m. p. 188—189° (Found: C, 58·2; H, 4·7; N, 11·1. $C_{24}H_{22}O_9N_4$ requires C, 58·3; H, 4·5; N, 11·3%).

2 : 4-*Diphenylpyrrolidine*.—2 : 4-Diphenylpyrroline (5 g.) in ethanol (20 ml.) was hydrogenated in presence of Raney nickel W.7 (1 g.). After filtration and removal of ethanol *in vacuo*, the oily residue (5 g.) was converted into its picrate (m. p. 132—138°), and the base regenerated. The hydrochloride of the base gave needles (from methanol), m. p. 170—171° (Kohler and Drake [1] give m. p. 171—172°). Similarly hydrogenation of 2 : 4-di-*p*-methoxyphenylpyrroline gave the pyrrolidine as an oil, which yielded a *picrate* as yellow needles (from ethanol), m. p. 181—182° (Found: C, 56·2; H, 4·9; N, 10·6. $C_{24}H_{24}O_9N_4$ requires C, 56·3; H, 4·7; N, 10·9%).

Preparation of 3 : 5-*Diaryl*-2-*methylpyrrolines*.—Reduction of the isomeric nitroethane–chalcone adducts was effected by method (a) or (b) above, see Table.

Preparation of 3 : 5-*Diaryl*-2-*methylpyrrolidines*.—3-*p*-Methoxyphenyl-2-methyl-5-phenylpyrroline A (5 g.) in ethanol (30 ml.) was hydrogenated in presence of Raney nickel W.7. (1 g.), 1 mol. of hydrogen being taken up. The product was filtered and evaporated *in vacuo*. The resulting oil (4·3 g., 86%) was converted into a *picrate*, which crystallised from benzene in needles, m. p. 205—206° (Found: C, 57·8; H, 4·5; N, 11·0. $C_{24}H_{24}O_9N_4$ requires C, 58·1; H, 4·9; N, 11·3%). The *base* was obtained from the picrate as above, as an oil, n_D^{20} 1·5610

[17] Rupe and Gisiger, *Helv. Chim. Acta*, 1925, **8**, 338.

XUM

(Found: C, 81·2; H, 8·1; N, 4·9. $C_{18}H_{21}ON$ requires C, 80·9; H, 7·9; N, 5·2%). Isomer B gave an isomeric 3-p-*methoxyphenyl*-2-*methyl*-5-*phenylpyrrolidine*, n_D^{20} 1·5480 (Found: C, 81·3; H, 8·2; N, 5·1%), which yielded a *picrate*, needles (from benzene), m. p. 264—265° (Found: C, 58·2; H, 5·1; N, 11·6%).

3-Aryl-2-methyl-5-phenylpyrrolines.

		Starting		Yield			Found (%)				Required (%)		
No.	3-Aryl	ketone	Method	(%)	B. p./mm.	n_D^{20}	C	H	N	Formula	C	H	N
1	Ph	A	b; 70°	85	150—154°/0·9	1·5110	86·5	7·2	6·1	$C_{17}H_{17}N$	86·8	7·3	6·0
2	,,	B	,,	—	—	1·5100	86·2	7·4	5·8	,,	,,	,,	,,
3	*p*-MeO·C_6H_4	A	b; 50°	88	172—174°/0·1	1·5000	81·2	7·1	5·1	$C_{18}H_{19}ON$	81·5	7·2	5·3
4	,,	B	,,	—	180—183°/1·5	—	81·6	6·9	5·5	,,	,,	,,	,,
5	*p*-Tolyl	A	a	80	190—195°/0·8	—	86·5	7·4	5·3	$C_{18}H_{19}N$	86·7	7·7	5·6
6	,,	B	a	—	200—205°/1	—	86·4	7·4	5·7	,,	,,	,,	,,

Picrates

			Found (%)				Required (%)		
No.	Form	M. p.	C	H	N	Formula	C	H	N
1	Plates [a]	149—150°	59·1	4·6	12·0	$C_{23}H_{20}O_7N_4$	59·5	4·3	12·1
2	,,	145—146 [b]	59·2	4·9	12·2	,,	,,	,,	,,
3	,,	168—169	58·2	4·7	11·5	$C_{24}H_{22}O_9N_4$	58·3	4·5	11·3
4	,,	171—172 [c]	57·9	4·5	11·1	,,	,,	,,	,,
5	Needles	200—201	60·5	4·2	11·5	$C_{24}H_{22}O_7N_4$	60·2	4·6	11·7
6	Plates	190—191	59·9	4·3	11·4	,,	,,	,,	,,

[a] From C_6H_6. [b] Mixed with no. 1, 120—130°. [c] Mixed with no. 3, 150—155°.

Similarly catalytic hydrogenation of isomer A of 2-methyl-5-phenyl-3-*p*-tolylpyrroline gave a 2-*methyl*-5-*phenyl*-3-p-*tolylpyrrolidine* (91%), n_D^{20} 1·5100 (Found: C, 86·4; H, 7·9; N, 5·8. $C_{18}H_{19}N$ requires C, 86·7; H, 7·7; N, 5·6%), which gave a *picrate*, needles (from benzene), m. p. 145—146° (Found: C, 60·5; H, 4·9; N, 11·8. $C_{24}H_{22}O_7N_4$ requires C, 60·2; H, 4·6; N, 11·7%). The isomeric *base* had n_D^{20} 1·5670 (Found: C, 86·4; H, 7·4; N, 5·3%) and gave a *picrate*, needles (from ethanol), m. p. 118—119° (Found: C, 60·5; H, 4·5; N, 11·9%).

5-*Ethoxycarbonyl*-2 : 4-*diphenylpyrroline* was obtained by hydrogenation of the nitro-ketone ester by method (a) above as a syrup (86% yield) (Found: C, 78·1; H, 6·6; N, 4·7. $C_{19}H_{19}O_2N$ requires C, 77·8; H, 6·5; N, 4·8%) and gave a *picrate*, needles, m. p. 155—156° (Found: C, 57·6; H, 4·1; N, 10·7. $C_{25}H_{22}O_9N_4$ requires C, 57·3; H, 4·2; N, 10·7%).

Hydrogenation of the pyrroline ester in ethanol with Raney nickel W.7 gave the *pyrrolidine*, n_D^{20} 1·5520 (Found: C, 77·7; H, 7·4; N, 4·4. $C_{19}H_{21}O_2N$ requires C, 77·3; H, 7·2; N, 4·7%) [*picrate*, needles, m. p. 128—129° (Found; C, 57·1; H, 4·5; N, 10·8. $C_{25}H_{24}O_9N_4$ requires C, 57·3; H, 4·6; N, 10·7%)].

The ester (1 g.) was refluxed with 2N-hydrochloric acid (6 ml.) for 2 hr. The solution was concentrated under reduced pressure to 2 ml. Aqueous ammonia was added and the product extracted with benzene. Water-washing and removal of the benzene gave the *pyrrolidine-acid* as a gum (0·7 g., 78%) (Found: C, 74·9; H, 5·4; N, 5·5. $C_{17}H_{15}O_2N$ requires C, 77·0; H, 5·6; N, 5·2%), whose *picrate* formed needles (from ethanol), m. p. 184—185° (Found: C, 55·7; H, 3·8; N, 11·4. $C_{23}H_{18}O_9N_4$ requires C, 55·8; H, 3·7; N, 11·3%).

We are grateful to Miss E. M. Tanner, Parke Davis & Co., Hounslow, Middlesex, for determining the infrared spectra and for suggestions on their interpretation.

THE POLYTECHNIC, 309, REGENT ST., LONDON, W.1. [*Received, November 25th*, 1957.]

XUM

461. *Metal Carbonyl Compounds. Part IV.* An Infrared Spectroscopic Investigation of Some Platinum(II) and Palladium(II) Carbonyl Compounds.*

By R. J. Irving and E. A. Magnusson.

The relation between the bond properties of bonds M–A and A–B in various metal–ligand systems M–A–B has been examined, and the relevance of force constant data to the problem of metal–ligand bond properties is discussed. C–O, N–H, and Pt–N stretching frequencies for a number of carbonyl complexes of platinum and palladium are reported and discussed in connection with the configurations and *trans*-effects of the various ligands and the stabilities and structures of the complexes containing them.

Force constants derived from the stretching vibrational frequencies of bonds A–B in metal–ligand systems M–A–B (where M = metal) have been used by several investigators as a measure of the properties of the metal–ligand bond M–A.[1,2] The relation between the bonds A–B and M–A in complex compounds is usually only vaguely understood and various assumptions about it have been made in interpretation of spectroscopic data of this type.

It is well known that the " true " stretching force constant of a bond is an excellent indication of the strength of attachment of the vibrating atoms. In practice, however, it is difficult to assess the effect on the stretching frequency of interaction with other vibrational modes of the molecule, or to assign correctly the different types of frequencies which may occur. Except in a few isolated cases (*e.g.*, the binary carbonyls [3]) use of stretching frequencies to calculate absolute force constants and bond strengths is unwarranted for these reasons alone, and it should be restricted to comparison with analogous systems. It is possible to correct stretching frequencies for " mechanical " (stretch-stretch) interaction with adjacent bonds, and in systems where large variations in stretching frequencies occur these corrections can be very important [4] and should be considered in any comparison.

Though there is an obvious need for further study of M–A–B systems where both M–A and A–B stretching frequencies are simultaneously observable, knowledge now suffices for a preliminary appraisal of the method. Metal–ligand systems of this kind fall into two main types: (i) either or both of the M–A and A–B bonds are pure σ-bonds (*e.g.*, in metal hydrates, ammines); and (ii) conjugation occurs between the M–A and the A–B bond (*e.g.*, in metal carbonyls, cyanide complexes). In general the A–B frequency shifts of complexes of the first type reflect only weakly the corresponding changes in the M–A bonds in a series of compounds, and the latter changes are in many cases considerable.

In a recent study [2] of a number of metal ammines—the type of complex most frequently examined spectroscopically—the metal–nitrogen frequencies have been compared with the nitrogen–hydrogen frequencies. Some of these results, and some from the present investigation, are given in Table 1. The maximum variation of the mean N–H stretching frequency in a large series of complexes of the type *trans*-[L,am $PtCl_2$] is only 15 cm.$^{-1}$, corresponding to a change in the force constant of only ~1% where the corresponding Pt–N force constant varies by approximately 10%.[2b] Some of the larger variations of the N–H frequency shown in Table 1 arise because of different types of N–H vibration, and the frequencies are then not comparable, though they are comparable, for example, in nos. 4, 5, and 6, where the environments of the vibrating atoms are the same. The

* Part III, *J.*, 1957, 2018.

[1] Chatt, Duncanson, and Venanzi, *J.*, 1955, 4461; Irving and Magnusson, *J.*, 1957, 2018.
[2] (*a*) Powell and Sheppard, *J.*, 1956, 3105; (*b*) Powell, *J.*, 1956, 4495.
[3] King and Lippincott, *J. Amer. Chem. Soc.*, 1956, **78**, 4192.
[4] (*a*) Nyholm and Short, *J.*, 1953, 2673; (*b*) Magnusson, Thesis, Sydney, 1957.

XUM

large variations between the frequencies for compounds 7, 8, and 9 undoubtedly arise from hydrogen-bonding interaction with the anion. Because of hydrogen bonding, O–H frequencies in hydroxy-compounds and hydrates are often difficult to interpret but a few compounds have been examined.[5] In azide and *iso*thiocyanate complexes N–N and C–N frequency variations are small between complexes of the same metal, but they may differ appreciably in other cases.

TABLE 1. *Stretching frequencies of metal complexes of σ-bonding ligands.*

No.	Compound		Frequencies		Ref.
1	*trans*-$[(C_2H_4)(NH_3)PtCl_2]$[a]	481	Pt–N; 3300	N–H	2*b*
2	*trans*-$[(Et_2S)(NH_3)PtCl_2]$[a]	493	Pt–N; 3170, 3200	N–H	2*b*
3	*trans*-$[(NH_3)_2PtCl_2]$[a]	507	Pt–N; 3170, 3270	N–H	2*b*
4	*trans*-$[(CO)(C_7H_7{\cdot}NH_2)PtCl_2]$[a]	488	Pt–N; 3257, 3319	N–H	*a*
5	*trans*-$[(CO)(C_7H_7{\cdot}NH_2)PtBr_2]$[a]	492	Pt–N; 3251, 3312	N–H	*a*
6	*trans*-$[(CO)(C_7H_7{\cdot}NH_2)PtI_2]$[a]	493	Pt–N; 3248, 3309	N–H	*a*
7	$[Co(NH_3)_6]Cl_3$		*ca.* 3070	N–H	*b*
8	$[Co(NH_3)_6Br_3$		*ca.* 3120	N–H	*b*
9	$[Co(NH_3)_6]I_3$		*ca.* 3150	N–H	*b*

[a] This investigation. [b] Fujita, Nakamoto, and Koboyashi, *J. Amer. Chem. Soc.*, 1956, **78**, 3295.

Small variations are to be expected in type (i) systems since the very nature of the bonding precludes any serious change in A–B bonding. " Mesomeric " effects should be largely inoperative and " inductive " effects [6] appear to be only weakly transmitted through the X–M–A–B systems, paralleled by the minor shifts produced in N–H frequencies of aromatic primary amines by inductive substituents in the ring.

A–B frequencies in type (ii) systems should be much more sensitive to changes in M–A bond type and bond order owing to the contributions of both forms (I) and (II) to the structure. The availability of π-electrons in systems involving structures (I) and (II) is such that the π-bond orders are very roughly complementary and, in a series of analogous

(I) M–A≡B M=A=B (II)

compounds, an increase in either the M–A or the A–B frequency is accompanied by an appreciable decrease in the other. Of course, A–B σ-bonds are unlikely to be affected by inductive effects any more than they are in type (i) systems, but there is still a greater contribution by inductive modification of the more easily polarisable π-electrons.

Reported work on A–B frequencies of this type generally supports the suggested relation between M–A and A–B bonds, [3,4,7] though much of the work has been on isolated compounds rather than on series containing comparable M–A–B systems.

Platinum Carbonyl Compounds.—In an effort to provide more information on both M–A and A–B bonds in series of compounds of a particular metal we have examined the infrared spectra of numerous platinum carbonyl compounds in the range where Pt–C stretching frequencies could be expected (600—250 cm.$^{-1}$) but have been unable to locate any band. Because of their colour few of the compounds can be studied by Raman spectroscopy and even where this was possible again no band capable of unequivocal assignment could be observed.

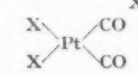
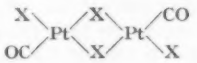
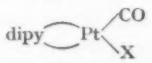
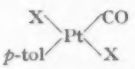
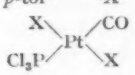
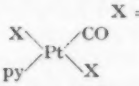
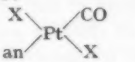
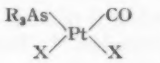
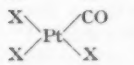
The C–O stretching frequencies of a number of chloro-, bromo-, and iodo-complexes of platinum(II) containing carbon monoxide and various other ligands are listed in Table 2. Except in the case of the dicarbonyl complex (*a*) each co-ordination entity exhibited only one band in the region 1800—2300 cm.$^{-1}$. The positions of the bands, which were very strong and sharp, were unaffected by the physical state of the samples.

Table 2 shows that the variations between the chloro-, bromo-, and iodo-complexes are predominantly due to " inductive " effects. The same order is observed in each of the horizontal series, the shifts being in the opposite order to those expected from mesomeric weakening of the Pt–C bond where the effects of the halogens are in the order

[5] Fujita, Nakamoto, and Koboyashi, *J. Amer. Chem. Soc.*, 1956, **78**, 3963.
[6] Chatt, Duncanson, and Venanzi, *J.*, 1956, 4456.
[7] Hawkins, Mattraw, Sabol, and Carpenter, *J. Chem. Phys.*, 1955, **23**, 2422.

I > Br > Cl, and therefore νC–O (iodo-complex) > νC–O (bromo-complex) > νC–O (chloro-complex). "Orbital contraction," discussed by Craig and Magnusson,[8] should give a reliable indication of the "inductive effects" of these ligands. For this case, the effective nuclear charge on the platinum atom might be expected to be increased by charge increments in the approximate ratio 5 : 4 : 3 for the interactions of chlorine, bromine, and iodine respectively. For compounds of this type, an increase in the effective nuclear charge should lead to bond weakening and the effects of the halogens should thus be in the order Cl > Br > I, and νC–O (chloro-complex) > νC–O (bromo-complex) > νC–O (iodo-complex). This order is observed in each of the horizontal series of C–O frequencies in Table 2 (*i.e.*, for X = Cl, Br, I in each complex [(CO)LPtX$_2$]).

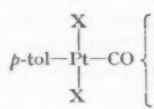
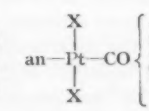
TABLE 2. C–O *Stretching frequencies* (*cm.*$^{-1}$) *of platinum carbonyl complexes.*

		X = Cl	Br	I
(*a*)		2200 2162	—	—
(*b*)		2146	2135	2122
(*c*)		2145	2132	2120
(*d*)		2136	2129	2120
(*e*)		2135	2130	2103
(*f*)		2135	2130	2119
(*g*)		2132	2128	2117
(*h*)		2111	2106	2092
(*i*)		2106	2096	2076

dipy = 2 : 2′-dipyridyl, py = pyridine, an = aniline, *p*-tol = *p*-toluidine.

Additional evidence for the assignment of the horizontal νC–O shifts to the relative "inductive effects" of the halogens is obtained from the νN–H and νPt–N shifts of complexes of the same type where L is an ammine. The C–O, N–H, and Pt–N frequencies of some of these are given in Table 3. Assignments of the Pt–N frequencies follow those made for analogous compounds by Powell.[2b] Although different amines are involved mesomeric electron-withdrawal by the CO group *trans* to the amine may be partly responsible for the shift in Pt–N frequencies (~490 cm.$^{-1}$) relative to those observed [2b] for ammine complexes which do not contain groups of high *trans*-effect (~510 cm.$^{-1}$).

TABLE 3. N–H, C–O, *and* Pt–N *frequencies* (*cm.*$^{-1}$) *of some platinum carbonyl ammines.*

		X = Cl	Br	I
	N–H (symm.)	3257	3251	3248
	N–H (asymm.)	3319	3312	3309
	C–O	2136	2129	2120
	Pt–N	488	492	493
	N–H (symm.)	3257	3254	3248
	N–H (asymm.)	3319	3315	3309
	C–O	2132	2128	2117
	Pt–N	—	481	482

Superimposed on this are the shifts obviously due to the "inductive effects" of the halogen in the *cis*-positions. The shifts in the N–H frequencies occur in the opposite direction [Pt–N: 488 ⟶ 493; N–H (mean) 3288 ⟶ 3279] as expected, but they correspond to much smaller changes in the force constant. Comparison of the spectra of these *p*-toluidine complexes with those of the type *trans*-[*p*-tolLPtCl$_2$] (where L = PR$_3$, SbR$_3$, C$_2$H$_4$, SR$_2$, SeR$_2$, etc.) [1] again shows that the effect of "mesomeric" electron-withdrawal is not transmitted far enough to produce shifts in νN–H comparable to those in νPt–N.

The vertical shifts in C–O frequency in Table 2 are attributed to the various "inductive"

[8] Craig and Magnusson, *J.*, 1956, 4895.

XUM

and " mesomeric " effects of the ligands but it is difficult to separate these contributions. The large shift (about 40 cm.$^{-1}$) between compounds (*b*) and (*i*) indicates that the bonding of bridging halogen atoms is quite different from that of terminal halogen. If inductive effects alone were operating, frequencies even lower than those of the compounds (*i*) would be expected for the bridged compounds because of the slightly greater bond lengths of the bridging halogens. It has been suggested that in some molecules *d*-orbitals may be involved in both σ- and π-bonds to halogen atoms.[9] Such a suggestion in this context would be purely speculative but such bonding should be favourable on overlap grounds in view of the fairly large effective nuclear charges which have been postulated.

The extreme rapidity of attack on these bridged complexes by nucleophilic groups, compared with attack on mononuclear complexes (see Part III) also suggests that contributions to the bond strength from platinum π-type orbitals are important here.

N–H frequencies of halogen-bridged ammine complexes are not available and comparison of the effect of terminal and bridging halogen atoms in this case is not possible.

The very high C–O frequencies of the dicarbonyl complex *cis*-$[Pt(CO)_2Cl_2]$ indicate considerable weakening of the Pt–C bond relative to that in the other complexes. Bond weakening due to the chlorine atoms might be expected to be less important here than in the case of the ions (*i*) since there are only two halogens present. It should be noted however, that π-bonding is possible between both the p_z and p_y orbitals of the carbon and the platinum π-type orbitals.[10] Bonding of this type, involving π-components in both the *z* and the *y* direction (the *x* direction being taken through the Pt–C σ-bond), should enhance the bond strength of a single Pt–C–O system by setting up an almost axially symmetrical conjugated Pt–C–O system similar to that in the carbon dioxide molecule. This would not be so if the overlap of the carbon p_z orbital with the $5d_{xz}6p_z$ hybrid of the platinum atom is so important relatively to the overlap of the carbon p_y with the unhybridized $5d_{xy}$ that the bonding is predominantly in the favour of the former, as is sometimes supposed. Overlap calculations seem to indicate that the admixture of the $6p_z$ and $5d_{xz}$ platinum orbitals does not increase bond strength enough to eliminate the possibility of bonding in the *y* direction.[4b] Thus, a *cis*-mesomeric effect, resulting from competition of the two CO groups for platinum d_π-orbitals in the plane of the four σ-bonds, is not only possible but in all probability quite important, the variation in Pt–C bond strength between the compounds (*i*) and the dicarbonyl compound (*a*) being considerable. It is obvious that, though carbon monoxide is only very weakly bonded, the various contributions to the bond strength are each important, though individually small.

Decomposition of Platinum Carbonyl Complexes.—The complicated mechanisms of decomposition by heat and moisture of these compounds have been mentioned by several authors. The stability to heat of the dimers $[Pt(CO)X_2]_2$ increases in the order $Cl < Br < I$, while the stabilities to moisture follow the reverse order.[11,12] In general the dimeric compounds are more sensitive to moisture than the monomeric derivatives, the notable exception being the dicarbonyl compound [1,12] $[Pt(CO)_2Cl_2]$. The behaviour of these compounds to both moisture and heat is difficult to reconcile to relative Pt–C bond strengths as indicated by the spectroscopic data.

Reaction of the dimeric complexes with water results in the liberation of carbon monoxide and carbon dioxide, the relative amounts varying a great deal with the conditions (temperature, relative proportions of water and complex, state of division of the compound, etc.). The proportion of the carbonyl compound actually decomposed (and thus the amount of carbon monoxide and dioxide liberated) is not constant and varying amounts of $[Pt(CO)X_3]^-$ are usually recovered. The latter probably result from the reaction of

[9] Mulliken, *J. Amer. Chem. Soc.*, 1955, **77**, 884.
[10] Craig, Maccoll, Nyholm, Orgel, and Sutton, *J.*, 1954, 332.
[11] Harris, Nyholm, and Stephenson, *Nature*, 1956, **177**, 1127; Manchot, *Ber.*, 1925, **58**, 2518.
[12] Emeléus and Anderson, " Modern Aspects of Inorganic Chemistry," George Routledge and Sons, Ltd., London, 1938, p. 406.

as-yet-unchanged $[Pt(CO)X_2]_2$ with the dilute hydrohalic acids produced from the liberation of the hydrogen halides according to the equations: [12]

$$H_2O + [Pt(CO)X_2]_2 \longrightarrow Pt + 2HX + CO_2$$
$$2X^- + [Pt(CO)X_2]_2 \longrightarrow 2[Pt(CO)X_2]^-$$

A semiquantitative determination of the CO_2 : CO ratio for the reaction of water with the various carbonyl compounds was made by carrying out the decompositions in a gas cell fitted with rock-salt windows and examining the infrared spectra after reaction. In general, the more violent the reaction, the greater the proportion of carbon dioxide. Analogous results were obtained when the substances were decomposed by means of ethyl alcohol, acetone, and even diethyl ether, although the reactions were usually less violent, especially in the case of the ether.[4b] With the exception of $[Pt(CO)_2Cl_2]$ none of the carbonyl complexes liberates carbon monoxide on treatment with the hydrohalic acids, but the pH of the decomposing agent does not appear to be the most important factor. Although solutions containing the hydroxide ion cause rapid decomposition, it is noteworthy that neutral solutions of halide ions appear to prevent liberation of carbon monoxide just as well as do solutions of the corresponding acids. It may be that the stability of these complexes in the presence of halide ions is explained by the postulate of the formation of 6-covalent halogen complexes sufficiently robust to prevent attack of the platinum atom. Complexes of this type appear to be reasonably common with platinum(II) though few have been isolated in the solid state.[11]

Palladium Carbonyl Complexes.—An attempt was made to resolve some of the difficulties apparent in the literature of the carbonyl complexes of palladium, but in spite of great care it was not possible to obtain any of the compounds examined in a sufficiently pure state to permit complete characterization. Infrared spectroscopy, however, was reasonably informative.

The compound $Pd(CO)Cl_2$, first reported by Manchot [11] has been assumed to be analogous to $[Pt(CO)Cl_2]_2$, a halogen-bridged dimer. It is extremely sensitive to heat but is only comparatively slowly attacked by moisture. Anderson produced the compound [12] [Pd(CO) en Cl][$Pd(CO)Cl_3$], by reaction of ethylenediamine with $Pd(CO)Cl_2$. This type of compound is well known as the product of the reaction of bidentate ligands with halogen-bridged platinum compounds. However, Gelman and Meilakh [13] considered Anderson's compound to be the ethylenediammonium salt of the anion $[Pd_2(CO)_2Cl_4]^{2-}$ although their preparation of the compound was carried out by an entirely different method from different starting materials. We repeated their preparation, namely, by the action of carbon monoxide on a saturated solution of ammonium chloropalladite in hydrochloric acid. A copious yellow precipitate was formed over a period of a week. The time for precipitation could be reduced to a few hours if the carbon monoxide was under moderate pressure.

This yellow precipitate was very unstable when dry, and surface decomposition to palladium was rapid. The partially decomposed product was diamagnetic and it absorbed strongly in the infrared region at 1920 ± 15 cm.$^{-1}$, showing a very wide band. The supposed ethylenediammonium salt prepared from the yellow product by the addition of ethylenediamine hydrochloride absorbed at 2056 cm.$^{-1}$, showing conclusively that the ligand produces a marked change in the structure of the complex and does not merely act as a cation. As a check, ethylenediamine hydrochloride was added to a solution of $[Pd(CO)Cl_2]_2$ in hydrochloric acid, and the spectrum of the resulting precipitate measured. This precipitate and that resulting from the action of anhydrous ethylenediamine on an acetone solution of $Pd(CO)Cl_2$ gave spectra identical with that of Gelman and Meilakh's compound, the infrared absorption being centred at 2056 ± 2 cm.$^{-1}$ in each case. This, and the fact that the absorption of the dimeric $[Pd(CO)Cl_2]_2$ occurs at 1976 cm.$^{-1}$, lead to the conclusion that the yellow compound obtained by Gelman and Meilakh

[13] Gelman and Meilakh, *Compt. rend. Acad. Sci. U.R.S.S.*, 1939, **24**, 748.

XUM

was actually $NH_4^+[Pd(CO)Cl_3]^-$, which reacted with ethylenediamine to give $[Pd(CO)\ en\ Cl]^+[Pd(CO)Cl_3]^-$, as also did the dimer. Each of these reactions is to be expected by analogy with the behaviour of the corresponding platinum complexes.

Experimental

The preparations of the compounds $[Pt(CO)LX_2]$ all involved the action of molar quantities of ligand on the dimeric complexes $[Pt(CO)X_2]_2$. Details are recorded in Parts I [14] and III [1] of this series.

Spectroscopic data were obtained by means of a double-beam single-pass spectrometer for the rock-salt region (νC–O). The instrument was designed and built in the Physical Chemistry Department of the N.S.W. University of Technology. Calibration was accomplished by a polystyrene film. Compounds were measured in the solid state as paraffin mulls and in many cases the measurements were repeated on 1% CCl_4 solutions. On no occasion was there any significant difference between the solid and the solution spectrum.

The spectra in the lithium fluoride (νN–H) and cæsium bromide (νPt–N) regions were obtained on a double-pass single-beam Perkin-Elmer model 112 spectrometer. Calibration in the lithium fluoride region was made from the standard water vapour bands, and in the cæsium bromide region from iodobenzene. The 20° cæsium bromide prisms enabled a lower limit of 250 cm.$^{-1}$ to be reached, and bands separated by as little as 8 cm.$^{-1}$ could be resolved. Measurements in the lithium fluoride region were made on 0·005—0·02M-carbon tetrachloride solutions of the complexes. Thick paraffin mulls supported between cæsium bromide plates were used in the cæsium bromide region.

Department of Chemistry, New South Wales University of Technology,
Broadway, New South Wales, Australia. [*Received, January 6th*, 1958.]

[14] Irving and Magnusson, *J.*, 1956, 1860.

---

462. *Reactions of Organic Peroxides. Part IX.* Hydroperoxides of Some Alkyltetralins.*

By B. Yeomans and Donald P. Young.

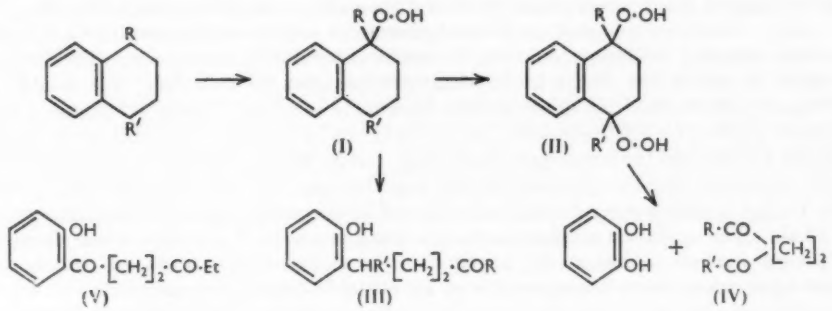
1 : 4-Dimethyl- and 1 : 4-diethyl-tetralin are each easily oxidised successively to the 1-monohydroperoxide and two stereoisomeric 1 : 4-dihydroperoxides. 1-Ethyltetralin similarly yields the 1-hydroperoxide and small amounts of an unstable 1 : 4-dihydroperoxide. Acid-cleavage of the dihydroperoxides gives catechol and diketones; the monohydroperoxides give the expected keto-phenols.

1-Methyltetralin was oxidised to its 1-hydroperoxide by Hock, Depke, and Knauel [1] who experienced some difficulty in carrying out the oxidation at 45°. We find that 1-ethyl-, 1 : 4-dimethyl-, and 1 : 4-diethyl-tetralin are all oxidised easily and rapidly with oxygen at 90°, suitably in presence of dilute alkali solution. These cyclic hydrocarbons absorb oxygen much more readily than the corresponding alkylbenzenes. Comparative maximum rates of absorption (for the hydrocarbons emulsified with one-quarter of their volumes of 2·5% aqueous sodium carbonate at 90°) are: 1-ethyltetralin 10, 1 : 4-diethyltetralin 12, 1 : 4-dimethyltetralin 18, 1 : 1 : 3-trimethylindane [2] 10, *m*-di*iso*propylbenzene 4 mol. % per hr., and *o*-di*iso*propylbenzene [3] 0. The difference between 1 : 4-dimethyltetralin and the substantially unoxidisable *o*-di*iso*propylbenzene is especially

* Part VIII, *J.*, 1956, 4785.

[1] Hock, Depke, and Knauel, *Chem. Ber.*, 1950, **83**, 238.
[2] Webster and Young, *J.*, 1956, 4785.
[3] Distillers Co. Ltd., Hawkins, Quin, and Salt, B.P. 641,250/1950.

striking, and demonstrates the large effect of immobilising the oxidisable carbon atom in a ring. The increased sensitivity of hydrogen atoms to radical attack when they are attached to a cyclic carbon atom appears to be a general phenomenon, probably arising from a combination of entropy factors, facilitation of resonance in the resulting free radical, and prevention of steric hindrance between bulky rotatable groups. The effect has been discussed by Russel,[4] who considers that the bond dissociation energy of a C–H bond (where the carbon atom is in the α-position to an ethylenic or aromatic carbon) is lowered when the carbon atom is incorporated in a 6-membered ring. He calculated that the C–H bond in the α-position in tetralin is 5·6 kcal./mole weaker than in *iso*propylbenzene. Since a tertiary C–H bond is 3—4 kcal./mole weaker than a secondary one, the difference between the α-C–H bond strengths in a 1-alkyltetralin and an *iso*alkylbenzene would be roughly 9 kcal./mole.

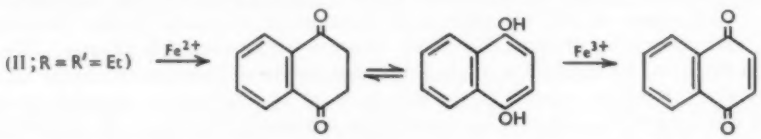


The dialkyltetralins could be oxidised to 80—100% conversion at about 80% efficiency in respect of oxygen to hydroperoxide. They initially formed monohydroperoxides (I; R = R′ = Me or Et), the constitution of which was confirmed by their acid-cleavage to ketophenols (III). Continued oxidation led to dihydroperoxides (II). The latter were soluble in dilute aqueous sodium hydroxide and were separated from the oxidation mixture by this means; the monohydroperoxides were not appreciably soluble in aqueous sodium hydroxide of any concentration, but they passed from the dihydroperoxide-free product in light petroleum into aqueous-methanolic sodium hydroxide. In each case, two isomeric dihydroperoxides were obtained, although only the higher-melting and less soluble ones were obtained pure. Diethyltetralin gave one solid isomer, which crystallised from chloroform or toluene with solvent of crystallisation, probably held in a clathrate structure (compounds with bulky 1 : 1-disubstitution on a bicyclic skeleton appear to be prone to form clathrate compounds). The other isomer did not solidify. Both dihydroperoxides from dimethyltetralin were crystalline, but not solvated. Each pair of isomers gave the same acid-cleavage products, and they were evidently *cis*- and *trans*-isomers. Similar stereoisomerism might be expected with the monohydroperoxides, but was not definitely observed. The starting hydrocarbons appeared to be homogeneous.

The planar formula (II; R = R′ = Et), with both hydroperoxide groups attached to tertiary carbon atoms, was proved by reduction of the dihydroperoxide to what was clearly 1 : 4-diethyl-1 : 4-dihydroxytetralin, since it readily eliminated water to give 1 : 4-diethylnaphthalene. Further, acid-cleavage of the dihydroperoxides (II; R = R′ = Me or Et) gave catechol and a diketone (IV). From 1 : 4-diethyl-1 : 4-dihydroperoxytetralin the yields of these were poor, and a third product, $C_{12}H_{14}O_3$, was also formed. This was phenolic and possessed two keto-groups of differing reactivities, and thus was *o*-4-oxohexanoylphenol (V) formed by irregular cleavage at one of the hydroperoxide centres.

[4] Russel, *J. Amer. Chem. Soc.*, 1955, **77**, 4583.

Ferrous sulphate converted the dihydroperoxides (II; R = R′ = Et) into 1 : 4-naphthaquinone in small yield, presumably by the route shown.



1-Ethyltetralin was oxidised similarly, giving mainly a tertiary monohydroperoxide (I; R = Et, R′ = H), which was extracted from the oxidate by means of aqueous-methanolic sodium hydroxide; we did not observe any special instability towards alkali such as was encountered by Hock *et al.*[1] in the case of 1-methyltetralyl hydroperoxide. Acid-cleavage of this hydroperoxide proceeded normally, giving the product (III; R = Et, R′ = H). Continued oxygenation of the hydrocarbon led to small amounts of a dihydroperoxide, although oxidation could not be carried beyond 50% conversion. The dihydroperoxide, in which one of the hydroperoxy-groups must be secondary, was soluble in, but rapidly decomposed by, dilute sodium hydroxide solution. It was precipitated from the crude product by light petroleum, but it could not be purified. Insufficient crystalline material was obtained to investigate its cleavage, but an impure dihydroperoxide isolated by alkali extraction gave catechol and the phenolic diketone (V); the latter may have arisen from 1-ethyl-1-hydroperoxy-4-oxotetralin formed by decomposition of the dihydroperoxide by alkali. The oxidation residues contained small amounts of a ketone which, from the m. p. and analysis of derivatives, appeared to be 4-ethyl-1-oxotetralin. If this is so it would have arisen from decomposition of an unstable 4-monohydroperoxide.

Experimental

The remarks on handling peroxides in Part VIII [2] apply equally here. " Light petroleum " refers to the grade of b. p. 40—60°.

Materials.—1-Ethyltetralin,[5] b. p. 240·0°/760 mm., n_D^{20} 1·5520, d_4^{20} 0·9547, and 1 : 4-diethyltetralin, b. p. 266·5°/760 mm., n_D^{20} 1·5262, d_4^{20} 0·9433, were kindly supplied by Ethyl Corp., New York. 1 : 4-Dimethyltetralin was prepared according to Colonge and Pichat's directions;[6] 5-phenylhexan-2-one was conveniently hydrogenated to the alcohol over copper–chromium oxide at 160°/50 atm., rapidly and quantitatively: the hydrocarbon boiled at 231·5°/749 mm., and had n_D^{20} 1·5297, and no change of b. p., n_D, or infrared spectrum during fractionation through a 50-plate column. Our constants differ appreciably for those recorded [7] for the *cis*-hydrocarbon of unstated provenance.

Oxidation of 1 : 4-*Diethyltetralin.*—The hydrocarbon (400 g., 2·13 moles) and 2·5% aqueous sodium carbonate (100 ml.) were vigorously stirred in oxygen at 90° for 14 hr., by which time 1·47 moles of oxygen had been taken up and 1·10 equiv. of hydroperoxide formed. Benzene (400 ml.) was added, whereupon some solid dihydroperoxide crystallised and was filtered off. The aqueous layer was rejected, and the liquid organic phase was extracted with 2N-sodium hydroxide (4 × 150 ml.).

The alkaline extract was neutralised with carbon dioxide, then shaken with benzene, and the whole filtered. The rest of the " solid " 1 : 4-*diethyl*-1 : 4-*dihydroperoxytetralin* (II; R = R′ = Et) was thereby removed [the combined solid products amounted to 21 g. (0·20 equiv. of hydroperoxide)]. This recrystallised from chloroform as a solvate, m. p. 104—107° (sealed tube; rapid heating) (Found: dihydroperoxide, by titration, 75·3; loss in wt. at 78°/0·1 mm., 19·0%), or from toluene as a solvate, m. p. 105—108° (sealed tube; rapid heating) (Found: dihydroperoxide, 80·6; loss in wt., 13·2, 13·5%). When heated slowly in an open tube, these solvates melted indefinitely at about 115°. They lost solvent in 1 hr. at 78°/0·1 mm., or in a few days

[5] Ethyl Corp., B.P. 766,215/1957.
[6] Colonge and Pichat, *Bull. Soc. chim. France*, 1949, 853, 855.
[7] Dreisbach, " Physical Properties of Chemical Compounds," Amer. Chem. Soc., 1955, p. 251.

in the atmosphere, leaving the solvent-free dihydroperoxide, m. p. 120° (Found: C, 66·9; H, 7·8%; iodometric equiv., 127, 131. $C_{14}H_{20}O_4$ requires C, 66·7; H, 8·0%; equiv., 126). The benzene layer of the filtrate, when washed, dried and evaporated *in vacuo*, left the crude "liquid" dihydroperoxide as a viscous oil, assaying 77% of diethyldihydroperoxytetralin by titration. It could not be purified further.

The alkali-extracted products from several oxidations were combined and the benzene was removed under reduced pressure below 50°. The residue was diluted with thrice its volume of light petroleum, and extracted repeatedly with a mixture containing 200 g. of sodium hydroxide and 500 ml. of methanol per l., the rest being water. The alkaline extract was diluted and neutralised with carbon dioxide, and the liberated hydroperoxide collected in light petroleum. By repeated recrystallisation from light petroleum, 1 : 4-*diethyl*-1-*hydroperoxytetralin* was obtained as needles, m. p. 63—64° (Found: C, 75·8; H, 8·8%; equiv., 214. $C_{14}H_{20}O_2$ requires C, 76·3; H, 9·1%; equiv., 220. The analysis suggested that it still contained a little dihydroperoxide).

A purer sample of hydrocarbon was oxidised to 100% absorption at 79% efficiency. The oxidation by-products were mainly a mixture of ketones.

Acid-cleavage of 1 : 4-*Diethyl*-1 : 4-*dihydroperoxytetralin*.—The "liquid" dihydroperoxide (II; R = R′ = Et) (16·3 g., 72% pure) in acetone (80 ml.) was added during 5 min. to sulphuric acid (0·1 g.) in boiling acetone (80 ml.). After the mixture had been boiled for 40 min., all the peroxide had disappeared. The product was neutralised and concentrated as previously, and partitioned between carbon tetrachloride (or benzene) and water. The aqueous layer yielded 1·52 g. (30%) of catechol, m. p. 104—106°, accompanied by some tar. The carbon tetrachloride layer was extracted twice with 2N-sodium hydroxide (75 ml.), whence acidification precipitated an oil which was isolated by means of ether and then lixiviated with hot light petroleum. The extract, on cooling, deposited waxy plates of o-4-*oxohexanoylphenol* (V), m. p. 39·5—40°, b. p. 115—125°/0·1 mm. (1·67 g.) (Found: C, 70·0; H, 7·0. $C_{12}H_{14}O_3$ requires C, 69·9; H, 6·8%) (for derivatives see below). The alkali-extracted carbon tetrachloride layer, on being washed and distilled, afforded octane-3 : 6-dione (1·41 g., 22%), m. p. 34—36°, b. p. 106—112°/25 mm., and material, b. p. up to 170°/25 mm. (2·82 g.). The diketone (for which Blaise [8] recorded b. p. 98°/14 mm., m. p. 34—35°) was characterised as 1-anilino-2 : 5-diethylpyrrole,[9] m. p. 67° (lit., 65·5°), and 2 : 5-diethyl-1-*p*-nitrophenylpyrrole,[10] m. p. 96° (lit., 95—96°).

The "solid" isomer of the dihydroperoxide gave the same products in similar yields. Various other acid catalysts were tried, without improvement in yields.

Characterisation of o-4-*Oxohexanoylphenol* (V).—The infrared spectrum showed the general characteristics of an *o*-disubstituted aromatic compound, a saturated open-chain ketone (1718 cm.$^{-1}$), and an *o*-hydroxyphenyl ketone (1640 cm.$^{-1}$). As with other compounds containing the •C(OH):C•CO• structure,[11] the hydroxyl absorption was only just detectable as a broad weak band superimposed on the CH band. The substance was strongly fluorescent in ultraviolet light. Warming the compound with one equiv. of hydroxylamine hydrochloride and sodium acetate in aqueous ethanol for 1 hr. afforded the *monoxime*, m. p. 103—108°; the m. p. was unsharp after repeated recrystallisation from light petroleum or 50% ethanol, and the oxime may have been a mixture of isomers (Found: C, 65·0; H, 6·8; N, 6·1. $C_{12}H_{15}O_3N$ requires C, 65·1; H, 6·8; N, 6·1%). The *dioxime* was obtained by heating the keto-phenol under reflux with a large excess of hydroxylamine hydrochloride in pyridine and ethanol. Recrystallised from benzene, it had m. p. 125—127·5° (Found: C, 60·5; H, 6·8; N, 11·5. $C_{12}H_{16}O_3N_2$ requires C, 61·0; H, 6·8; N, 11·8%).

Other ketonic derivatives prepared in the usual way were the *monosemicarbazone*, m. p. 157—158° (from ethanol) (Found: C, 59·6; H, 6·6; N, 16·5. $C_{13}H_{17}O_3N_3$ requires C, 59·3; H, 6·5; N, 16·0%), and the orange *mono*-2 : 4-*dinitrophenylhydrazone*, m. p. 167—169° (from chloroform) (Found: N, 14·9. $C_{18}H_{18}O_6N_4$ requires N, 14·5%).

The 3 : 5-*dinitrobenzoate* had m. p. 130—132° (from ethanol or acetone) (Found: C, 57·1; H, 4·0. $C_{19}H_{16}O_8N_2$ requires C, 57·0; H, 4·0%). The *methyl ether*, prepared by means of methyl iodide and aqueous-methanolic sodium hydroxide, had b. p. 143°/0·5 mm. (Found: C, 70·7; H, 7·4. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%).

[8] Blaise, *Compt. rend.*, 1914, **158**, 506.
[9] *Idem*, *ibid.*, 1920, **171**, 34.
[10] Fetizon and Baranger, *ibid.*, 1953, **236**, 1428.
[11] Bellamy, "Infra-red Spectra of Complex Molecules," Methuen, London, 1954, p. 91.

XUM

Acid-cleavage of 1 : 4-*Diethyl*-1-*hydroperoxytetralin* (I; R = R′ = Et).—The monohydroperoxide (I; R = R′ = Et) by treatment with sulphuric acid in acetone, as described above, gave 6-o-*hydroxyphenyloctan*-3-*one* (64%), m. p. 34—35·5°, b. p. 195°/15 mm. (Found: C, 76·4; H, 8·7. $C_{14}H_{20}O_2$ requires C, 76·3; H, 9·2%). This depressed the m. p. of the diketo-phenol (V). A number of derivatives were prepared, but none crystallised; the oily 1-naphthylurethane yielded a pale orange *naphthylurethane* 2 : 4-*dinitrophenylhydrazone*, m. p. 167—169° (from benzene–ethanol) (Found: C, 65·2; H, 5·5; N, 12·8. $C_{31}H_{32}O_6N_5$ requires C, 65·4; H, 5·5; N, 12·3%).

Action of Ferrous Sulphate on 1 : 4-*Diethyl*-1 : 4-*dihydroperoxytetralin*.—To the solid dihydroperoxide (II; R = R′ = Et) (20 g.) in ethanol (150 ml.) was added ferrous sulphate heptahydrate (60 g.) in water (600 ml.), the temperature being kept below 30°. After an hour the mixture was warmed to 50° for an hour and then to the b. p. for a further hour. Concentrated hydrochloric acid (50 ml.) was added to dissolve the ferric hydroxide. The organic product, isolated by extraction with ether, was naphtha-1 : 4-quinone (2 g.), m. p. 124·5—125·5° (lit., 125°). The orange mono-2 : 4-dinitrophenylhydrazone had m. p. 264—268° (decomp.) [lit.,[12] 278° (decomp.)] (Found: C, 57·2; H, 3·3. Calc. for $C_{16}H_{10}O_5N_4$: C, 56·7; H, 3·0%).

Hydrogenation of 1 : 4-*Diethyl*-1 : 4-*dihydroperoxytetralin*.—The solid isomer of the dihydroperoxide (II; R = R′ = Et) in methanol was hydrogenated at room temperature and pressure over 0·7% palladium–alumina. The theoretical amount of hydrogen was absorbed. Removal of catalyst and solvent left 1 : 4-*diethyl*-1 : 4-*dihydroxytetralin*, which was recrystallised from benzene–light petroleum and then carbon tetrachloride to m. p. 93—94° (Found: C, 76·2; H, 9·0. $C_{14}H_{20}O_2$ requires C, 76·3; H, 9·2%).

This diol (1·0 g.) in boiling benzene in the presence of a trace of toluene-*p*-sulphonic acid eliminated water which was removed azeotropically. The washed evaporated solution yielded 1 : 4-diethylnaphthalene, identified by its ultraviolet spectrum and its *picrate*, yellow needles (from ethanol), m. p. 93—95° (Found: C, 57·9; H, 4·6. $C_{14}H_{16}.C_6H_3O_7N_3$ requires C, 58·1; H, 4·6%) (Arnold and Barnes [13] found m. p. 91—93°, but did not analyse their picrate).

Oxidation of 1 : 4-*Dimethyltetralin*.—The hydrocarbon (247 g., 1·56 mole) was oxidised in the manner described above. After 7 hr., 1·40 moles of oxygen had been absorbed, and 1·15 equivalents of hydroperoxide had been formed. Absorption was still proceeding rapidly at this point. The products were worked up as described before, except that as the dihydroperoxide was completely soluble in benzene the filtrations were omitted. The hydroperoxide fraction was obtained as a solid (25 g.) which melted over a wide range. Recrystallisation from chloroform afforded a sharp-melting 1 : 4-*dihydroperoxy*-1 : 4-*dimethyltetralin* (II; R = R′ = Me), m. p. 149—150° (decomp.) (Found: C, 64·1; H, 7·1%; iodometric equiv., 111. $C_{12}H_{16}O_4$ requires C, 64·2; H, 7·2%; equiv., 112). The mother-liquors were diluted with light petroleum, and the precipitate recrystallised repeatedly from toluene and then benzene, yielding a dihydroperoxide melting indefinitely at about 90°. The hydroperoxide titre of this eventually fell to 79% of the theoretical, showing that decomposition was occurring. 1 : 4-*Diethyl*-1-*hydroperoxytetralin* was obtained as a viscous oil which could not be distilled without decomposition (Found: C, 75·0; H, 8·5%; equiv., 209. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·4%; equiv., 192).

Acid-cleavage of 1 : 4-*Dimethyltetralin Hydroperoxides*.—The method already described was used. A mixture of the dihydroperoxide (II; R = R′ = Me) isomers (92% pure) gave catechol (100%) and hexane-2 : 5-dione (31%), identified as its phenylhydrazone, m. p. and mixed m. p. 116—118°. The pure dihydroperoxide isomer, m. p. 150°, gave 71% of catechol (estimated in the aqueous extract as lead iodate [14]).

Cleavage of the monohydroperoxide (I; R = R′ = Me) yielded 5-o-*hydroxyphenylhexan*-2-*one* (III; R = R′ = Me) (28·7 g.), b. p. 130—135°/0·3 mm., n_D^{20} 1·5330 (supercooled), m. p. 42—44° (from light petroleum) (Found: C, 74·8; H, 8·3. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·4%). The *semicarbazone*, crystallised from ethanol, had m. p. 175—176° (Found: C, 62·9; H, 7·7; N, 16·5. $C_{13}H_{19}O_2N_3$ requires C, 62·7; H, 7·7; N, 16·9%). The dinitrophenylhydrazone and benzoate were not crystalline.

Oxidation of 1-*Ethyltetralin*.—(*a*) The hydrocarbon (400 g., 2·50 moles) and 2·5% aqueous sodium carbonate (100 ml.) were oxygenated at 90° for 9·75 hr. After 6·5 hr., 40 mol. % of

[12] Roduta and Quibilan, *Rev. filip. Med. Farm.*, 1936, **27**, 123.
[13] Arnold and Barnes, *J. Amer. Chem. Soc.*, 1944, **66**, 960.
[14] Baernstein, *J. Biol. Chem.*, 1945, **161**, 684.

oxygen had been absorbed, 95% of which had been converted into hydroperoxide, but beyond this time the hydroperoxide content did not increase despite further absorption of oxygen. The product was diluted with an equal volume of light petroleum, and the aqueous phase rejected. Extraction with 2N-sodium hydroxide removed 0·14 equiv. of hydroperoxide; the extract was very dark. Neutralising it with carbon dioxide liberated an oil (*A*) which was collected with light petroleum and did not crystallise (15·0 g.); titration showed an iodometric equivalent of 202, corresponding to 54% purity as dihydroperoxide, and to a total of only 0·07 equiv.; therefore half the hydroperoxide had been lost during neutralisation. The alkali-washed organic phase was next extracted with a mixture (divided into 3 parts) of 80 g. of sodium hydroxide and 400 ml. of methanol made up to 800 ml. with water. The hydroperoxide (*B*), regenerated from this extract in the usual way, formed a viscous oil assaying 85·2% as mono-hydroperoxide (I; R = Et, R′ = H).

(*b*) The organic phase from a similar oxidation was dried, diluted with a large volume of light petroleum, and cooled to −80°. The gummy precipitate was repeatedly dissolved in benzene and precipitated with light petroleum, finally being brought to m. p. 118—119° [depressed by (II; R = R′ = Et)], then assaying as 83% dihydroperoxide (II; R = Et, R′ = H). Attempts to purify it further were unsuccessful; it amounted to less than 1 g.

Distillation of oxidation residues after removal of all hydroperoxide afforded a small amount of ketonic material, b. p. 128°/13 mm. to 95°/0·3 mm., which appeared to be mainly 4-ethyl-1-oxotetralin; it yielded an *oxime*, m. p. 80—81° (Found: C, 75·9; H, 8·0; N, 6·9. $C_{12}H_{15}ON$ requires C, 76·1; H, 8·0; N, 7·4%), semicarbazone, m. p. 182·5—183° (Found: N, 18·1. Calc. for $C_{13}H_{17}ON_3$: N, 18·2%), and scarlet 2 : 4-*dinitrophenylhydrazone*, m. p. 198—200° (Found: C, 61·1; H, 4·9; N, 16·3. $C_{18}H_{18}O_4N_4$ requires C, 61·1; H, 5·1; N, 15·8%). Levy [15] records a m. p. of 183° for the semicarbazone.

Acid-cleavage of 1-*Ethyltetralin Hydroperoxides*.—The dihydroperoxide concentrate (*A*) mentioned above (14·4 g.) gave, by the usual procedure, catechol (0·28 g.) and *o*-4-oxohexanoylphenol (V) (1·37 g), m. p. and mixed m. p. 35—38°. Distillation of the neutral part of the product gave no definite fraction.

Cleavage of the monohydroperoxide concentrate (*B*) required 80 min. at reflux temperature, and yielded 6-o-*hydroxyphenylhexan*-3-*one*, b. p. 196—198°/22 mm., n_D^{20} (supercooled) 1·5322, m. p. 32—33° (Found: C, 74·5; H, 8·0. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·4%). Its pale orange 2 : 4-*dinitrophenylhydrazone* had m. p. 136—137° (from aqueous alcohol and then benzene) (Found: C, 57·8; H, 5·2; N, 15·4. $C_{18}H_{20}O_5N_4$ requires C, 58·1; H, 5·4; N, 15·0%).

Thanks are offered to Ethyl Corp. for the gift of 1-ethyl- and 1 : 4-diethyl-tetralin, to Messrs. A. R. Philpotts and W. F. Maddams for the spectroscopic work, and to Mr. B. Gnyra for fractionating hydrocarbons.

THE DISTILLERS CO. LIMITED, RESEARCH AND DEVELOPMENT DEPT.,
GREAT BURGH, EPSOM, SURREY. [*Received, January 9th*, 1958.]

[15] Levy, *Compt. rend.*, 1933, **197**, 772.

XUM

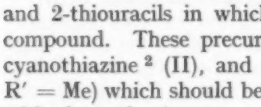
463. *Purines, Pyrimidines, and Glyoxalines. Part IX.* Syntheses of Uridine, 2-Thiouridine, and Some Related Compounds.*

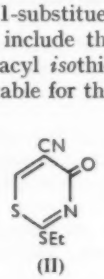
By G. Shaw, R. N. Warrener, and (in part) (Miss) M. H. Maguire and R. K. Ralph.

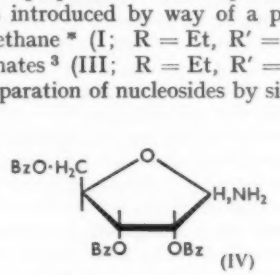
Uridine, 5-cyanouridine, 2-thiouridine, 5-methyl-2-thiouridine, and 5-cyano-2-thiouridine have been prepared by reaction of acrylamides (I), acyl *iso*thiocyanates (III), or the cyanothiazine (II) with 2 : 3 : 5-tri-*O*-benzoyl-D-ribosylamine (IV) and debenzoylation of the products. The apparent exclusive formation of β-glycosides in these reactions is discussed.

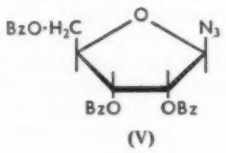
In Part II [1] of this series we described an unambiguous synthesis of 1-substituted pyrimidine nucleosides, by reaction of several D-glycosylamines (1-amino-1-deoxy-sugars or tautomers thereof) with the acrylamides (I; R = Et, R′ = CN, R″ = H or Me). Periodate titrations of these nucleosides showed that they had the pyranose configuration, and their specific rotations suggested the β-glycosidic configuration.

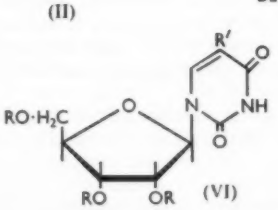
In other Parts of this series we described the preparation of some precursors of uracils and 2-thiouracils in which a 1-substituent is introduced by way of a primary amino-compound. These precursors include the urethane [*] (I; R = Et, R′ = R″ = H), the cyanothiazine [2] (II), and the acyl *iso*thiocyanates [3] (III; R = Et, R′ = H; and R = R′ = Me) which should be suitable for the preparation of nucleosides by similar reactions with glycosylamines.

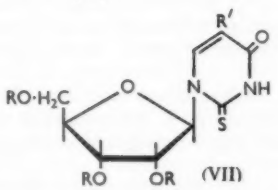












Application of our methods to the synthesis of pyrimidine nucleosides related to the ribofuranosides of natural origin required β-D-ribofuranosylamine or a suitable derivative thereof. Such a compound, 2 : 3 : 5-tri-*O*-benzoyl-D-ribosylamine (IV), has recently been prepared by catalytic hydrogenation of 2 : 3 : 5-tri-*O*-benzoyl-β-D-ribosyl azide (V) obtained from the ribosyl halide and sodium azide in methyl cyanide.[4] The method is an extension of one used by Bertho for the preparation of 2 : 3 : 4 : 6-tetra-*O*-acetylglucosyl azide and D-glucosylamine.[5]

From its method of preparation, the ribosylamine (IV) would formally be expected to have the β-configuration. However, the isolation of α- and β-glycyl derivatives of the amino-sugar [4] suggests that mutarotation occurs readily and that the ribosylamine is perhaps best regarded as an αβ-mixture.

Reaction of the ribosylamine (IV) with the acrylamide (I; R = Et, R′ = R″ = H) in

* Part VIII, *J.*, 1958, 157.

[1] Ralph and Shaw, *J.*, 1956, 1877.
[2] Atkinson, Shaw, Schaffner, and Warrener, *J.*, 1956, 3847.
[3] Shaw and Warrener, *J.*, 1958, 153.
[4] Baddiley, Buchanan, Hodges, and Prescott, *Proc. Chem. Soc.*, 1957, 148; *J.*, 1957, 4769.
[5] Bertho, *Ber.*, 1930, **63**, 836.

ethyl acetate, in the presence of triethylamine, and debenzoylation of the product with methanolic sodium methoxide gave uridine (VI; R = R′ = H), the identity of which was confirmed by comparison with an authentic specimen. Only one other synthesis of uridine has been recorded,[6] by deamination of cytidine which was prepared by the Hilbert–Johnson method [7] from acetobromoribofuranose and 2 : 6-diethoxypyrimidine and then reaction of the product with ammonia.

The similar reaction of the ribosylamine with the acrylamide (I; R = Et, R′ = CN, R″ = H) and the cyanothiazine (II) gave crystalline tri-*O*-benzoates (VI; R = Bz, R′ = CN) and (VII; R = Bz, R′ = CN) respectively. Debenzoylation as before then afforded 5-cyanouridine (VI; R = H, R′ = CN) and 5-cyano-2-thiouridine (VII; R = H, R′ = CN).

The acyl *iso*thiocyanate (III; R = R′ = Me) also readily afforded a crystalline tri-*O*-benzoate (VII; R = Bz, R′ = Me) but debenzoylation of this as above or with alcoholic ammonia gave non-crystalline material. Ultraviolet absorption spectra of the crude material and of material purified by elution from paper chromatograms and cellulose powder columns, were unlike those expected of a 1-substituted 2-thiouracil, but very similar to those of 1-substituted 2-alkylthio- or 2-alkoxy-pyrimidines, which show maximum absorption at about 245 mμ, unchanged in acid or alkaline solution.[8] These results are difficult to explain for, although thiouracils are known to undergo nucleophilic replacement reactions, these are confined to the 4-thio-derivatives. Thus, 2 : 4-dithiouracil when heated with ammonia or amines gives 2-thiocytosine and derivatives, replacement of sulphur occurring only in the 4-position.[9] In addition, in a model experiment, 1-methyl-2-thiothymine was recovered in good yield after treatment with methanolic sodium methoxide under conditions even more vigorous than those used for the tri-*O*-benzoate (VII; R = Bz, R′ = Me). The latter compound was eventually successfully converted into 5-methyl-2-thiouridine (VII; R = H, R′ = Me) by sodium hydroxide in aqueous, peroxide-free dioxan.

Reaction of the acyl *iso*thiocyanate (III; R = Et, R′ = H) with the ribosylamine (IV) and hydrolysis of the product with sodium hydroxide in aqueous dioxan similarly gave 2-thiouridine (VII; R = R′ = H).[10] Sodium methoxide gave results analogous to those with the 5-methyl derivative.

Confirmation of the structure of the 2-thiouridine was obtained by heating it for several hours with aqueous chloroacetic acid. Paper chromatography of the solution in butanol saturated with 3% aqueous boric acid gave spots corresponding to unchanged 2-thiouridine (R_F 0·3) and uridine (R_F 0·15). The latter material was eluted with buffer solutions, whose ultraviolet absorption was then identical with that of uridine at the same pH values.

Strominger and Friedkin [11] reported enzymic formation of a 2-thiouracil riboside on incubating together 2-thiouracil and ribose 1-phosphate with thymidine phosphorylase. This riboside was not obtained crystalline but was purified by elution from paper chromatograms with butanol saturated with 3% aqueous boric acid. Its identity as a 1-ribosyl-2-thiouracil followed from its stability to acid, its ultraviolet absorption in acid and alkaline solutions (where differences occur, characteristic of 1-substituted 2-thiouracils), and its enzymic arsenolysis to 2-thiouracil and ribose. By analogy with similar enzymic Kalckar syntheses,[12] it seemed likely that the substance was 2-thiouridine.

Our material appears to be very similar to that prepared by Strominger and Friedkin. The ultraviolet spectra (see Fig. 1) are identical with those reported for acid, neutral,

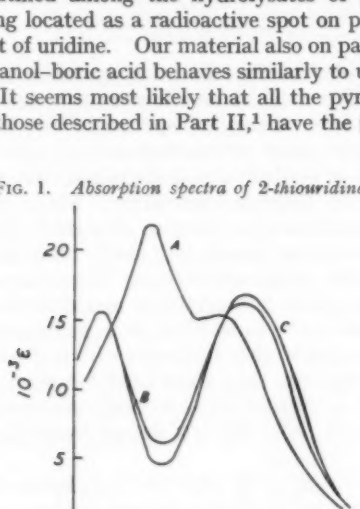
[6] Howard, Lythgoe, and Todd, *J.*, 1947, 1052.
[7] Hilbert and Johnson, *J. Amer. Chem. Soc.*, 1930, **52**, 2001, 4489.
[8] Shugar and Fox, *Bull. Soc. chim. belges*, 1952, **61**, 293.
[9] Hitchings, Elion, Falco, and Russell, *J. Biol. Chem.*, 1949, **177**, 357.
[10] Cf. Shaw and Warrener, *Proc. Chem. Soc.*, 1957, 351.
[11] Strominger and Friedkin, *J. Biol. Chem.*, 1954, **208**, 663.
[12] Kalckar, *Biochim. Biophys. Acta*, 1953, **12**, 250.

XUM

and alkaline solution except at wavelengths in the 220 mμ region where in our pure material we did not observe the enhanced absorption recorded for the enzymically prepared material, although such absorption was present in our less pure material. The R_F of our material in butanol saturated with 3% aqueous boric acid was about 0·3 which differs slightly from that recorded by Strominger and Friedkin for their material (0·25), but we regard this as of little significance since we have found that the solvent system used here does not readily give repeatable R_F values, although it is excellent for the separation of closely related nucleosides. A substance corresponding to 2-thiouridine has also been identified among the hydrolysates of [^{35}S]-2-thiouracil-treated tobacco mosaic virus,[13] being located as a radioactive spot on paper chromatograms, with an R_F value similar to that of uridine. Our material also on paper chromatography in solvent systems other than butanol–boric acid behaves similarly to uridine.

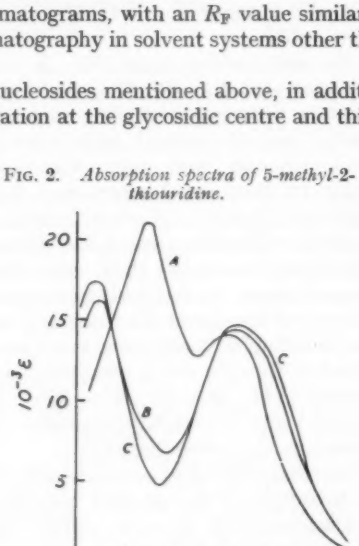
It seems most likely that all the pyrimidine nucleosides mentioned above, in addition to those described in Part II,[1] have the β-configuration at the glycosidic centre and this is

FIG. 1. *Absorption spectra of 2-thiouridine.*



A, 0·2M-K_2HPO_4, pH 9; *B*, M/15-Na_2HPO_4–M/15-KH_2PO_4 (4 : 1), pH 7·4; *C*, 0·01N-HCl.

FIG. 2. *Absorption spectra of 5-methyl-2-thiouridine.*



A, *B*, *C* as in Fig. 1.

confirmed by specific rotation values, and by analogy with the cases (uridine and 2-thiouridine) where additional proof is available. No isomeric α-glycosides have been detected among the products although their presence cannot be excluded.

In our experiments, pyrimidine formation in all cases must proceed through initial formation of linear intermediates of the type ribose–NH·CS·NH·CO·CR:CH·OR′ and ribose–NH·CH:CR′·CO·NH·CO_2Et and compounds of this type have been isolated when simple primary amines have been used (Part VIII and ref. 3).

An examination of molecular models suggests that cyclisation of the β-forms of these linear compounds should occur more readily than with the corresponding α-anomers which may accompany them. In the latter forms, the NH group is sterically hindered by the 2′-*O*-benzoyl group, and hindrance to cyclisation could be augmented by a tendency to oxazoline formation involving the reaction, $^-$NH + $^-$COPh ⟶ –N·CPh(OH)·.

Our results parallel the apparent exclusive formation in nature of the β-forms of pyrimidine and purine nucleosides, and it seems possible that the above remarks may provide a common explanation of these observations. Indeed one suggested route to pyrimidine nucleosides involves reactions and intermediates very similar to those described

[13] Mandel, Markham, and Matthews, *Biochim. Biophys. Acta*, 1957, **24**, 205.

in this paper.[14] In addition it has recently been shown that a ribofuranosylamine, namely, 5-phosphoribosylamine, is a precursor of purine nucleotides in biochemical systems,[15] and it seems likely that the same compound is concerned with biosynthesis of pyrimidine nucleotides.

Experimental

Dioxan was freed from peroxides by distillation from stannous chloride, and used immediately. Rotations were measured in water.

Uridine.—2 : 3 : 5-Tri-*O*-benzoyl-β-D-ribofuranosyl azide (1 g.) was reduced in dry " AnalaR " ethyl acetate (15 ml.) (ethyl acetate distilled from Raney nickel is also suitable), over a platinic oxide catalyst (0·1 g.) for 2 hr. Nitrogen produced during the reaction was removed by flushing the apparatus twice with hydrogen at intervals of about 45 min. To the dried (Na_2SO_4) filtered solution were added β-ethoxy-*N*-ethoxycarbonylacrylamide (0·5 g.) and triethylamine (1 ml.), and the mixture was boiled under reflux for 1 hr. The cooled solution was washed with dilute hydrochloric acid and water, dried, and evaporated to a gum. This was dissolved in methanol (10 ml.) containing a little sodium methoxide and set aside for 24 hr. The solvent was removed *in vacuo* and the residue dissolved in water and extracted with ether. The aqueous solution was treated with basic lead acetate solution, and the precipitated lead salt centrifuged off, washed with a little water, and methanol, then suspended in methanol and decomposed with hydrogen sulphide. Lead sulphide was removed, and the solution evaporated to a crystalline residue. Uridine (0·2 g.) separated from ethanol as needles, m. p. and mixed m. p. 165°, $[\alpha]_D$ +8° (*c* 1·5) (Found: C, 44·1; H, 5·1; N, 11·25. Calc. for $C_9H_{12}O_6N_2$: C, 44·25; H, 4·9; N, 11·45%).

2′ : 3′ : 5′-*Tri*-O-*benzoyl*-5-*cyanouridine.*—The ribosyl azide (1 g.) in ethyl acetate (100 ml.) was reduced as before. The filtered solution was treated with α-cyano-β-ethoxy-*N*-ethoxycarbonylacrylamide [16] (0·5 g.) and triethylamine (1 ml.), then boiled under reflux for 1 hr. The cooled solution was washed with dilute hydrochloric acid and water, dried, and evaporated to a gum. This was dissolved in warm ethanol (10 ml.) and set aside: an amorphous solid separated. This was removed and the filtrate evaporated to a small volume and kept at 0° overnight, a crystalline precipitate separating. 2′ : 3′ : 5′-*Tri*-O-*benzoyl*-5-*cyanouridine hemihydrate* (0·3 g.) separated from ethanol as needles, m. p. 190° (Found: C, 63·05; H, 4·15; N, 6·95. $C_{31}H_{23}O_9N_3,\frac{1}{2}H_2O$ requires C, 63·05; H, 4·1; N, 7·1%), $\lambda_{max.}$ 230 mμ (ε 38,400), 276 mμ (ε 13,200), λ_{min} 253 mμ (ε 5900) in EtOH.

5-*Cyanouridine.*—The preceding reaction was repeated and the product dissolved in methanol (10 ml.) containing sodium methoxide and set aside for 24 hr. The whole was worked up as for uridine, to give 5-*cyanouridine* (0·25 g.) as needles (from ethanol), m. p. 185°, $[\alpha]_D^{20}$ −6° (*c* 2·0) (Found: C, 44·5; H, 4·1; N, 15·75. $C_{10}H_{11}O_6N_3$ requires C, 44·6; H, 4·1; N, 15·6%), $\lambda_{max.}$ 276 mμ (ε 14,800) and 216 mμ (ε 13,000), $\lambda_{min.}$ 240 mμ (ε 2450) in H_2O. In 24 hr. at 18° the substance had consumed 1·05 mols. of 0·09N-sodium metaperiodate; no acid was formed in the reaction.

2′ : 3′ : 5′-*Tri*-O-*benzoyl*-5-*cyano*-2-*thiouridine.*—The ribosyl azide (3 g.) in ethyl acetate (250 ml.) was reduced over platinic oxide (0·3 g.) as before. The filtered solution was treated with 5-cyano-4-oxo-2-thio-1 : 3-thiazine (1·3 g.) and triethylamine (1 ml.) and boiled under reflux for 1 hr. The acid- and water-washed solution was dried and evaporated *in vacuo* to a gum. This was dissolved in warm benzene (15 ml.), and the solution set aside. 2′ : 3′ : 5′-*Tri*-O-*benzoyl*-5-*cyano*-2-*thiouridine* (1 g.) crystallised; it recrystallised from benzene as needles, m. p. 169° which retained benzene (Found, in material dried at 70°/0·1 mm.: C, 64·45; H, 4·0; N, 7·1. $C_{31}H_{23}O_8N_3S,\frac{1}{2}C_6H_6$ requires C, 64·15; H, 4·1; N, 6·6%. Found, in material dried at 120°/0·01 mm.: C, 63·3; H, 4·0. $C_{31}H_{23}O_8N_3S,\frac{1}{4}C_6H_6$ requires C, 63·2; H, 4·0%).

5-*Cyano*-2-*thiouridine.*—(*a*) The tribenzoate (0·5 g.) in methanol (20 ml.) containing a little sodium methoxide was kept overnight, then neutralised with acetic acid and evaporated *in vacuo* to dryness. The residue was dissolved in water and worked up as for uridine. 5-*Cyano*-2-*thiouridine* (0·12 g.) crystallised from ethanol as prisms, m. p. 185—186°, $[\alpha]_D^{18}$ +10° (*c* 1·0) (Found: C, 41·9; H, 4·1; N, 14·5. $C_{10}H_{11}O_5N_3S$ requires C, 42·1; H, 3·9; N, 14·75%), $\lambda_{max.}$ 300 mμ (ε 13,200), 271 mμ (ε 12,300), 223 mμ (ε 13,600) in H_2O; $\lambda_{max.}$ 291 mμ (ε 19,500), 267 mμ

[14] Mitchell and Houlahan, *Fed. Proc.*, 1947, **6**, 506.
[15] Goldthwaite, Greenberg, and Peabody, *Biochim. Biophys. Acta*, 1955, **18**, 148; Goldthwaite, *J. Biol. Chem.*, 1956, **222**, 1051.
[16] Shaw, *J.*, 1955, 1834.

XUM

(ε 14,500), 235 mμ (ε 18,400) in 0·2M-dipotassium hydrogen phosphate. (*b*) The tribenzoate (1 g.) in methanol (25 ml.) was treated with saturated methanolic ammonia (10 ml.), then set aside for 2 days. The solution was evaporated *in vacuo* and the residue extracted with ether. The remaining solid was dissolved in a little ethanol and seeded, to give after a few hours, 5-cyano-2-thiouridine (0·27 g.), m. p. and mixed m. p. 186°.

5-Cyano-2′ : 3′-isopropylidene-2-thiouridine.—The foregoing tribenzoate (0·7 g.) was debenzoylated as described in (*b*) above. The crude 5-cyano-2-thiouridine was shaken occasionally during 2 days with acetone (10 ml.), anhydrous copper sulphate (1 g.), and sulphuric acid (0·06 ml.). The mixture was filtered and the filtrate neutralised with solid sodium hydrogen carbonate. The solution was filtered and the filtrate evaporated to a solid residue. *5-Cyano-2′ : 3′-isopropylidene-2-thiouridine* (0·12 g.) separated from acetone–light petroleum (b. p. 40—60°) as needles, m. p. 189° (Found: C, 48·7; H, 4·65; N, 12·5. $C_{13}H_{15}O_5N_3S$ requires C, 48·0; H, 4·6; N, 12·9%).

2′ : 3′ : 5′-Tri-O-benzoyl-5-methyl-2-thiouridine.—The ribosyl azide (3 g.) in ethyl acetate (300 ml.) was reduced over platinic oxide (0·3 g.), and the filtered solution treated with β-methoxy-α-methylacryloyl *iso*thiocyanate (0·9 g.) and triethylamine (3 ml.). The solution was boiled under reflux for 1½ hr., cooled, and washed with N-hydrochloric acid (3 × 30 ml.) and water (5 × 30 ml.), dried, and evaporated *in vacuo* to a gum. When this was stirred with dry methanol (50 ml.) it rapidly crystallised. *2′ : 3′ : 5′-Tri-O-benzoyl-5-methyl-2-thiouridine* (1·61 g.) recrystallised from an excess of methanol as needles, m. p. 156—157°, which retained methanol (Found: C, 63·1; H, 5·15; N, 4·5. $C_{31}H_{26}O_8N_2S,\frac{1}{2}CH_3{\cdot}OH$ requires C, 62·8; H, 4·7; N, 4·65%), $\lambda_{max.}$ at 230 mμ (ε 40,900) and 262 mμ (ε 22,400), $\lambda_{infl.}$ 278 mμ (ε 20,400), $\lambda_{min.}$ 250 mμ (ε 17,900) in EtOH.

A solution of the tribenzoate (1 g.) in dry methanol (110 ml.) containing sodium methoxide (1 ml. of 1·9% solution in methanol) was boiled under reflux for 10 min., then set aside for 24 hr. The clear yellow solution was neutralised with Zeo-Karb 225 and evaporated to dryness *in vacuo*. The residue was treated with water which was then removed (accompanied by methyl benzoate) *in vacuo*. The residue was dissolved in water (20 ml.) and extracted with chloroform (3 × 7 ml.) and ether (10 ml.). Paper chromatography (ascending) of the aqueous solution in butanol saturated with water gave three absorbing spots with R_F 0·1, 0·2 (strong), and 0·5. The solution was evaporated and the residue chromatographed on a cellulose powder column, butanol saturated with water being used as solvent system. A main fraction (R_F 0·22) was isolated from the column as a brittle gum (Found: C, 35·4; H, 5·8; N, 11·1%), $\lambda_{max.}$ 242 mμ unchanged in acid or alkali. Similar results were obtained when the conditions were varied and when methanolic ammonia was used.

1-Methyl-2-thiothymine [3] (0·1 g.) in methanol (20 ml.) containing sodium (0·023 g.) was refluxed for 6 hr., then kept at room temperature for 3 days. The solution was neutralised with Zeo-Karb 225, warmed to dissolve a precipitate, and evaporated. Crystallisation of the residue from water gave 1-methyl-2-thiothymine (0·06 g.), m. p. and mixed m. p. 230°.

5-Methyl-2-thiouridine.—The foregoing tribenzoate (2·7 g.) in dioxan (30 ml.) was treated with 2N-sodium hydroxide (23 ml.) and water (6 ml.) to give a homogeneous solution, which was set aside for 24 hr., then neutralised with 2N-hydrochloric acid (23 ml.); an unpleasant mercaptan-like odour was apparent after addition of the acid. The solvent was removed *in vacuo* and the residue treated with water (50 ml.), and the precipitated benzoic acid removed with ether (3 × 30 ml.). The aqueous phase was evaporated to about 15 ml. and continuously extracted with ethyl acetate for 5 hr. The solution was cooled and set aside, giving a crystalline precipitate; *5-methyl-2-thiouridine* (0·45 g.) recrystallised from dry ethanol as needles, m. p. 217°, $[\alpha]_D^{26}$ +31° (*c* 1·23) (Found: C, 43·75; H, 4·9; N, 10·4. $C_{10}H_{14}O_5N_2S$ requires C, 43·8; H, 5·15; N, 10·2%). A further quantity of the nucleoside (0·15 g.) was recovered by evaporation of the ethyl acetate solution to dryness and crystallisation of the residue from ethanol. In butanol saturated with 3% aqueous boric acid the nucleoside had R_F 0·5, and in butanol–acetic acid–water (5 : 2 : 3) R_F 0·56 (ascending paper chromatography).

2-Thiouridine.—The ribosyl azide (3 g.) in ethyl acetate (300 ml.) was reduced over platinic oxide (0·3 g.), and the dried filtered solution treated with β-ethoxyacryloyl *iso*thiocyanate (0·9 g.) and triethylamine (3 ml.), then boiled under reflux for 2 hr. The acid- and water-washed solution was dried and evaporated *in vacuo* to a gum. This was dissolved in dioxan (40 ml.), and 2N-sodium hydroxide (15·4 ml.) and water (8·5 ml.) were added to give a homogeneous solution, which was set aside for 24 hr., then neutralised with 2N-hydrochloric acid

(15·4 ml.). The solution was evaporated to dryness *in vacuo*, then treated with water (50 ml.). Precipitated benzoic acid was removed by extraction with ether (3 × 30 ml.). The aqueous solution was then evaporated *in vacuo* to about 15 ml. and continuously extracted with ethyl acetate for 16 hr. The extract was evaporated to dryness *in vacuo* and the residual solid crystallised from aqueous ethanol, to give *2-thiouridine* (0·3 g.) as needles, m. p. 214°, $[\alpha]_D^{20}$ +39° (*c* 1·2) (Found: C, 41·4; H, 4·75; N, 10·6. $C_9H_{12}O_5N_2S$ requires C, 41·55; H, 4·65; N, 10·75%). In butanol saturated with 3% aqueous boric acid the nucleoside had R_F 0·3 (the value varied with the length of run and possibly with temperature, values being recorded to about 0·35), and in butanol–acetic acid–water (5 : 2 : 3) R_F 0·52. Uridine had R_F 0·47 in the latter solvent system and R_F about 0·15 in the former with variations to R_F 0·18 similar to those obtained with the thio-derivative.

Debenzoylation of the above reaction mixture with methanolic sodium methoxide or ammonia gave results similar to those obtained with the 5-methyl derivative.

Conversion of 2-Thiouridine into Uridine.—A solution of 2-thiouridine (5 mg.) in water (0·23 ml.) was heated on a water-bath, and chloroacetic acid (0·1 g.) was added in small portions at 8 hourly intervals. Ascending paper chromatography of the solution showed the presence of two absorbing spots (in butanol saturated with 3% aqueous boric acid), which corresponded to 2-thiouridine and uridine which were run at the same time. The reaction solution was run on paper as a strip, and the band corresponding to uridine cut out and divided into 2 parts, one of which was extracted with 0·2M-dipotassium hydrogen phosphate (pH 9·2) and the other with M/15-disodium hydrogen phosphate–M/15-potassium dihydrogen phosphate (4 : 1) (pH 7·4). Ultraviolet absorption spectra of these solutions were identical with those given by uridine in the same solvents with $\lambda_{max.}$ 262 mμ in each case and $\lambda_{min.}$ showing a characteristic change from 232 mμ (pH 7·4) to 239 mμ (pH 9·2). Calculations from known extinction coefficients for uridine indicated that the yield of uridine in the above reaction was approximately 15%. The synthetic uridine similarly had the same behaviour as the natural material when chromatographed on paper in butanol–acetic acid–water (5 : 2 : 3).

We thank the N.S.W. State Cancer Council for a research grant and Dr. E. Challen for microanalyses. Part of this work was carried out at the University Chemical Laboratories, Cambridge, by one of us (G. S.) during the tenure of a Nuffield Dominion travelling fellowship.

N.S.W. University of Technology,
Sydney, N.S.W., Australia. [*Received, December 10th*, 1957.]

---

464. *Purines, Pyrimidines, and Glyoxalines. Part X.* Synthesis of Uracil-6-phosphonic Acid, an Analogue of Orotic Acid.*

By (Miss) M. H. Maguire, R. K. Ralph, and G. Shaw.

Diethyl ethoxycarbonylacetylphosphonate (I) has been prepared by the reaction of triethyl phosphite with ethoxycarbonylacetyl chloride. With phenylhydrazine, the keto-ester gave the pyrazolone (II), and with urea and dry hydrogen chloride gave uracil-6-phosphonic acid (III).

Compounds structurally related to the pyrimidines and purines of nucleic acid origin, have proved important as growth-inhibitors of bacteria, viruses, and tumours. In the pyrimidine field, most of these compounds are sterically similar to uracil, thymine, and cytosine, and have been modelled on these pyrimidines by changes such as OH ⟶ SR, OH ⟶ NR_2, CH ⟶ N and by substitution of uracil in the 5-position by such substituents as halogen, NO_2, RO, NR_2. The inhibitory properties of the compounds are generally reversed by a naturally occurring pyrimidine and, in many cases, it appears that the analogues compete with the natural pyrimidines for a place in the nucleic acid molecule. These pyrimidine analogues may be classed as antimetabolites and examples are now known of their direct incorporation into the nucleic acid molecule.[1]

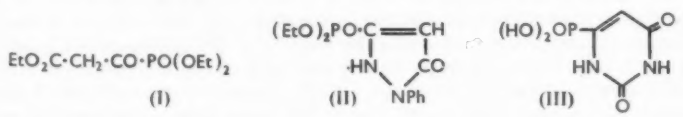
* Part IX, preceding paper.

[1] "The Nucleic Acids," Ed. Chargaff and Davidson, Academic Press, New York, 1955, and references therein; Matthews and Smith, *Adv. Virus Res.*, 1955, **3**, 49; Matthews, *Virology*, 1955, **1**, 165.

XUM

Among the naturally occurring pyrimidines, orotic acid (uracil-6-carboxylic acid) is of special importance. Although it is not known to be a constituent of nucleic acids it is nevertheless more readily incorporated into these acids, where it appears as uracil, than any of the normal pyrimidine constituents. If, as appears likely, growth-inhibition in this series is related to the degree of incorporation of the compound into the nucleic acid molecule, then analogues of orotic acid assume special interest. Very recently such analogues, 5-fluoro-orotic acid,[2] uracil-6-sulphonic acid,[3] and the corresponding sulphonamide and methyl sulphone,[4] have been found to have inhibitory activity towards lactobacilli and tumours.[5]

We now report the preparation of a further analogue, uracil-6-phosphonic acid (III), in which the carboxyl group of orotic acid has been replaced by a phosphonic acid group.



Triethyl phosphite reacted smoothly with ethoxycarbonylacetyl chloride to give the keto-ester (I). This gave a red colour with alcoholic ferric chloride, and its structure was confirmed by analysis, formation of a 2 : 4-dinitrophenylhydrazone, and reaction with phenylhydrazine to give the pyrazolone (II).

Preliminary attempts to cause the keto-ester to react with urea in alcoholic or non-polar solution in the presence of sodium methoxide were unsuccessful. The ester was peculiarly unstable in hydroxylic solvents in the presence of bases. When heated with anhydrous guanidine, it reacted readily, to give a crystalline compound with an ultraviolet absorption spectrum typical of 2 : 4-pyrimid-diones, but no satisfactory structure could be assigned to this substance. The required uracil-6-phosphonic acid was eventually readily obtained by the reaction of the ester (I) with urea in acetic acid in the presence of dry hydrogen chloride, conditions which are known to de-esterify phosphonic esters;[6] the acid (III) was isolated as a disodium salt, conversion of which into the free acid proved unexpectedly troublesome. Acidification of a concentrated solution of the sodium salt with hydrochloric acid precipitated a monosodium salt, which was also obtained when solutions of the disodium salt were treated with the acid form of Zeo-Karb 225. This behaviour is reminiscent of that shown by orotic acid which is frequently precipitated as its sodium salt from alkaline solution by acid. However, addition of an excess of silver nitrate to the disodium salt solution precipitated a trisilver salt (orotic acid gives a disilver salt), and decomposition of this with hydrogen sulphide afforded the free acid (III). The ultraviolet absorption spectra of the substance in acid, neutral, and alkaline solution were similar to those of orotic acid.

Experimental

Ethoxycarbonylacetyl chloride, b. p. 44°/2·5 mm., was prepared from dry potassium ethyl malonate and thionyl chloride in ether.[7] Commercial triethyl phosphite (Eastman Kodak) was redistilled, and a fraction of b. p. 43°/9 mm. used.

Diethyl Ethoxycarbonylacetylphosphonate.—Triethyl phosphite (50·14 g., 57·3 ml.) was added during 15 min., with shaking, to ethoxycarbonylacetyl chloride (50 g.) at 0°. The solution was

[2] Heidelberger, Chaudhuri, Danneberg, Mooren, Griesbach, Duschinsky, Schnitzer, Pleven, and Scheiner, *Nature*, 1957, **179**, 663; Duschinsky, Pleven, and Heidelberger, *J. Amer. Chem. Soc.*, 1957, **79**, 4559.
[3] Greenbaum and Holmes, *ibid.*, 1954, **76**, 2899.
[4] Greenbaum, *ibid.*, 1954, **76**, 6052.
[5] Hakala, Law, and Welch, *Proc. Amer. Assoc. Cancer Res.*, 1956, **2**, 113; Handschumaker and Welch, *Cancer Res.*, 1956, 965; Heidelberger, Mooren, Griesbach, Montag, Duschinsky, Pleven, and Schnitzer, *Proc. Amer. Assoc. Cancer Res.*, 1957, **2**, 212.
[6] Freedman and Doak, *Chem. Rev.*, 1957, **57**, 479.
[7] Staudinger and Becker, 1917, **50**, 1023.

then heated on a water-bath for 30 min. Vigorous evolution of ethyl chloride occurred and the solution became bright yellow. It was set aside at room temperature overnight, then distilled *in vacuo*, to give fractions, b. p. 40—100°/0·7 mm. (15 ml.) and b. p. 100—108°/0·7 mm. (49 g.), and a high-boiling residue. The main fraction was redistilled, to give *diethyl ethoxycarbonylacetyl phosphonate* (24·5 g.), b. p. 115°/0·9 mm. (Found: C, 43·0; H, 6·65. $C_9H_{17}O_6P$ requires C, 42·85; H, 6·8%). This slowly decomposed when repeatedly distilled. A solution of the ester in ethanol gave a ruby-red colour with ferric chloride solution. The 2 : 4-*dinitrophenylhydrazone* crystallised from aqueous ethanol as yellow needles, m. p. 77—78° (Found: C, 41·65; H, 4·7; N, 12·75. $C_{15}H_{21}O_9N_4P$ requires C, 41·65; H, 4·9; N, 12·95%).

Diethyl 5-Oxo-1-phenyl-Δ³-pyrazolin-3-ylphosphonate.—Freshly distilled phenylhydrazine (0·43 g.) and the acylphosphonate (1·1 g.) were mixed. When the initial exothermic reaction had subsided the mixture was heated on a water-bath for 1½ hr., to give a clear orange-coloured liquid. Some low-boiling material was removed *in vacuo* and the residue treated with N-sodium hydroxide; it partly dissolved. The insoluble oil was removed with ether, and the aqueous phase acidified with hydrochloric acid, to precipitate a dense orange oil. This was extracted into ether, and the solution dried, and evaporated to a gum (0·85 g.) which partly crystallised and was repeatedly crystallised from ethyl acetate–light petroleum, to give *diethyl 5-oxo-1-phenyl-Δ³-pyrazolin-3-ylphosphonate* (0·1 g.) as colourless plates, m. p. 89—91° (Found: C, 52·55; H, 5·8; N, 9·3. $C_{13}H_{17}O_4N_2P$ requires C, 52·7; H, 5·8; N, 9·45%). An alkaline solution of the pyrazolone with benzenediazonium chloride solution gave a vivid orange colour.

Reaction of the Acylphosphonate with Anhydrous Guanidine.—The phosphonate (10 g.) and anhydrous guanidine (3·2 g.), when mixed, became hot, viscous, and bright lemon-yellow. After the initial reaction, the solution was kept at 80° (bath) for 1½ hr., a solid being precipitated. This (3·9 g.) was extracted with ethanol–ether (2 : 1) and recrystallised from an excess of water, and then from aqueous acetic acid, to give colourless needles, m. p. >350° (Found: C, 42·55; H, 4·6; N, 16·85%), $\lambda_{max.}$ 280 mμ, $\lambda_{min.}$ 241 mμ in H_2O.

Uracil-6-phosphonic Acid.—A solution of the acyl phosphonate (2·52 g.) and urea (0·6 g.) in dry acetic acid (4·5 ml.) was heated on a water-bath, and dry hydrogen chloride passed through the solution during 30 min. The solution was set aside at 5° for 12 hr., then evaporated *in vacuo* to a gum. This was dissolved in ethanol (10 ml.) and treated with 10N-sodium hydroxide solution till the pH was 9—10. Crystals separated which were filtered off and washed with ethanol–water (3 : 1) and ethanol. *Disodium uracil-6-phosphonate dihydrate* (0·55 g.) recrystallised from aqueous ethanol as needles, m. p. >300° (Found: C, 17·3; H, 2·95; N, 10·6. $C_4H_3O_5N_2PNa_2,2H_2O$ requires C, 17·65; H, 2·6; N, 10·3%). Acidification of a concentrated solution of the disodium salt with 10N-hydrochloric acid precipitated a *hydrated monosodium salt* (Found: C, 20·25; H, 2·55; N, 11·7; P, 12·5%; equiv., 238. $C_4H_4O_8N_2PNa,1\frac{1}{2}H_2O$ requires C, 19·9; H, 2·9; N, 11·6; P, 12·85%; equiv., 241). The same compound was also obtained by evaporation of a solution of the disodium salt after it had been treated with Zeo-Karb 225 (acid form). Addition of an excess of silver nitrate solution to a solution of the disodium salt precipitated a *trisilver salt* (Found: C, 9·5; H, 1·0; N, 5·45 $C_4H_2O_5N_2PAg_3,1\frac{1}{2}H_2O$ requires C, 8·9; H, 0·95; N, 5·2%). The silver salt (0·15 g.) was suspended in water and decomposed with hydrogen sulphide. Silver sulphide was filtered off, and the filtrate evaporated *in vacuo*, to give *uracil-6-phosphonic acid monohydrate* (0·055 g.) as needles, m. p. 270° (decomp.) (Found: C, 22·8; H, 3·5; N, 13·05. $C_4H_5O_5N_2P,H_2O$ requires C, 22·85; H, 3·35; N, 13·35%), $\lambda_{max.}$ 265 mμ (ε 5880), $\lambda_{min.}$ 238 mμ (ε 2700) in 0·1N-NaOH; $\lambda_{max.}$ 267 mμ (ε 7200), $\lambda_{min.}$ 230 mμ (ε 840) in 0·1N-HCl; $\lambda_{max.}$ 264 mμ (ε 5400), $\lambda_{min.}$ 230 mμ (ε 1430) at pH 7.

We thank the N.S.W. State Cancer Council for a research grant, and Dr. E. Challen for microanalyses.

N.S.W. University of Technology,
Sydney, Australia.

[*Received, January 20th,* 1958.]

XUM

465. *Synthetic and Stereochemical Investigations of Reduced Cyclic Bases. Part V.* The Exhaustive Methylation of Some Partially Reduced Cyclic Bases.*

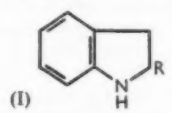
By H. Booth, F. E. King, and J. Parrick.

Decomposition of the *N*-methyl methohydroxides of 2 : 3-dihydro- and 2 : 3-dihydro-2-methyl-indole, of *cis*-1 : 2 : 3 : 4 : 10 : 11-hexahydro- and *cis*-1 : 2 : 3 : 4 : 10 : 11-hexahydro-11-methyl-carbazole, and of *cis*-1 : 2 : 3 : 3a : 4 : 8b-hexahydro*cyclo*pent[*b*]indole, results in the expected unsaturated *ortho*-substituted *NN*-dimethylanilines. The hydrogenation of tetrahydro*cyclo*pent[*b*]indole to the required hexahydro-derivative occurred almost quantitatively with Raney nickel catalyst, but reduction of the 1 : 2 : 3 : 4-tetrahydrocarbazole under a variety of conditions gave only poor yields of hexahydrocarbazole.

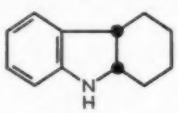
cis- and *trans*-1-Dimethylamino-2-*cyclo*hexyl*cyclo*hexane have been prepared by hydrogenation in acidic and alkaline media of the methine base from 1 : 2 : 3 : 4 : 10 : 11-hexahydrocarbazole, the structures of the products being confirmed by stereospecific syntheses from 2-*cyclo*hexyl*cyclo*hexanone.

Experiments on the synthesis and exhaustive methylation of several reduced cyclic bases described in Part I—IV have been extended to some incompletely saturated cyclic amines, more particularly those containing a 2 : 3-dihydroindole nucleus (I; R = H).

The dihydroindole system was considered by von Braun [1] to be one of the most resistant of the simpler cyclic amines to degradation by Hofmann exhaustive methylation, but no experimental results were presented in support of this conclusion. Fission of quaternary ammonium bases is a bimolecular elimination reaction,[2] and is therefore appreciably affected by substitution at the β-carbon atom, being impeded by the inductive effect of alkyl groups and assisted by the electromeric character of aromatic substituents at the β-



(I)



(II)

position. On theoretical grounds, therefore, the Hofmann degradation of 2 : 3-dihydroindoles should present no difficulties, and this has been confirmed by the formation of the expected *o*-dimethylaminostyrene from 1 : 1-dimethylindolinium hydroxide below 100° (experiments by K. G. Mason).

2 : 3-Dihydro-2-methylindole (I; R = Me) has twice been the subject of studies of this kind. In both cases [3,4] it is stated that distillation of the methohydroxide regenerates the dihydro-1 : 2-dimethylindole by expelling methanol, but the amine obtained was not identified by comparison with an authentic specimen. In the present investigation, a pure specimen of the *N*-methyl base (picrate, m. p. 128—130°) was prepared by distillation of 2 : 3-dihydro-1 : 2-dimethylindole methochloride. Hofmann fission of the amine methohydroxide proceeded smoothly at 70° and gave *NN*-dimethyl-*o*-propenylaniline (picrate, m. p. 168—170° compared with 158° recorded by von Braun *et al.*[4]), having ultraviolet absorption closely resembling that of *o*-dimethylaminostyrene. Hydrogenation of the unsaturated base over palladised charcoal gave *NN*-dimethyl-*o*-*n*-propylaniline giving a picrate of m. p. 176—178°, whereas for the picrate of the presumably

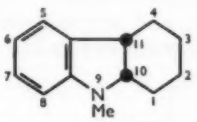
* Part IV, *J.*, 1954, 378.

[1] von Braun, *Ber.*, 1916, **49**, 2629; 1918, **51**, 96.
[2] Cf. Ingold, "Structure and Mechanism in Organic Chemistry," J. Bell and Sons, Ltd., London, 1953, p. 422.
[3] Bamberger and Sternitzki, *Ber.*, 1893, **26**, 1291.
[4] von Braun, Heider, and Neumann, *Ber.*, 1916, **49**, 2613.

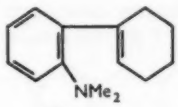
identical product obtained by Emde degradation of 2 : 3-dihydro-1 : 2-dimethylindole methochloride von Braun *et al.*[4] record m. p. 150°.

cis-Hexahydrocarbazole (II) is readily prepared by several methods,[5] and from the product obtained by reducing a large quantity of tetrahydrocarbazole with tin and hydrochloric acid Gurney, Perkin, and Plant [6] were able to isolate 1—2% of *trans*-hexahydrocarbazole. The configurations of the two isomers have not been rigidly proved but rest on the well-established generalisation that there is preferential formation of the less strained (*cis*) modification. Various methods for the preparation of hexahydrocarbazole have been re-examined in the hope of obtaining larger quantities of the *trans*-isomer for exhaustive methylation.

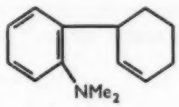
Hydrogenation of 1 : 2 : 3 : 4-tetrahydrocarbazole using catalysts of Raney nickel (60—120°) and copper chromite (160—170°) at 120 atm. initial pressure generally resulted in conversions into the hexahydro-derivative not exceeding 20%, thus broadly confirming the observations by Adkins and Coonradt.[7] The tetrahydro-*N*-methylcarbazole yielded 10% (with Raney nickel) and 15% (with copper chromite) of the corresponding hexahydrobase which however Adkins and Coonradt failed to obtain by hydrogenation of *N*-methylcarbazole. The more basic hexahydro-compound was isolated from the reaction mixture with dilute acid but even before recrystallisation it was apparent from m. p. determinations



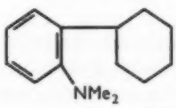
(III)



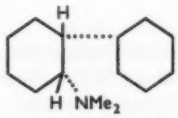
(IV)



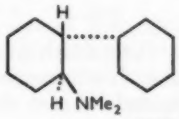
(V)



(VI)



(VII)



(VIII)

that the products were *cis*-base (II) with no significant content of the *trans*-isomeride. Reduction of tetrahydrocarbazole by nascent hydrogen, which in the case of tin and hydrochloric acid gave 1—2% of the *trans*-hexahydro-compound,[6] was therefore re-examined, and the possibility that the proportion of the two stereoisomers might be affected by pH led to the consideration of alkaline reducing agents. The reduction of carbazole to tetrahydrocarbazole by sodium and pentyl alcohol has been mentioned by a number of workers,[8,9] and it has been reported by Sanna [9] that prolonged reduction leads also to the formation of *cis*- and *trans*-hexahydrocarbazole. In our experiments, Sanna's method yielded only tetrahydrocarbazole; moreover, neither tetrahydrocarbazole nor tetrahydro-9-methylcarbazole gave any acid-soluble material after prolonged treatment with sodium and boiling pentyl alcohol. An attempted reduction of tetrahydro-9-methylcarbazole with lithium aluminium hydride was also unsuccessful (cf. Julian and Printy [10]). Further degradation studies were therefore restricted to the available *cis*-compounds.

Exhaustive methylation of *cis*-hexahydrocarbazole has been carried out by von Braun, Heider, and Neumann [4] who claimed that distillation of *cis*-hexahydro-9-methylcarbazole

[5] Graebe and Glaser, *Annalen*, 1872, **163**, 352; *Ber.*, 1872, **5**, 12; Schmidt and Sigwart, *Ber.*, 1912, **45**, 1779; Carrasco, *Gazzetta*, 1908, **38**, 303; Perkin and Plant, *J.*, 1924, 1503; Borsche, Bothe, and Witte, *Annalen*, 1908, **359**, 49; Clemo and Felton, *J.*, 1951, 700; Mears, Oakeshott, and Plant, *J.*, 1934, 272.

[6] Gurney, Perkin, and Plant, *J.*, 1927, 2676.

[7] Adkins and Coonradt, *J. Amer. Chem. Soc.*, 1941, **63**, 1563.

[8] Zanetti, *Ber.*, 1893, **26**, 2006; Schmidt and Schale, *Ber.*, 1907, **40**, 3225; Barclay, Campbell, and Gow, *J.*, 1946, 997.

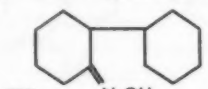
[9] Sanna, *Gazzetta*, 1950, **80**, 572.

[10] Julian and Printy, *J. Amer. Chem. Soc.*, 1949, **71**, 3206.

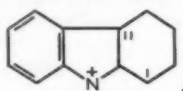
XUM

methohydroxide produced an oil consisting of the *N*-methyl base (III) contaminated with a small quantity of *o-cyclo*hex-1-enyl-*NN*-dimethylaniline (IV). In the present work, heating *cis*-hexahydro-9-methylcarbazole methohydroxide to *ca.* 90° caused decomposition exclusively to an unsaturated base, $C_{14}H_{19}N$, which was presumed to be (IV) or (V) and in the presence of palladised charcoal absorbed hydrogen to yield a dihydro-derivative (VI). The unsaturated base formed a methiodide only on prolonged refluxing with methyl iodide, thus exhibiting the usual low reactivity of *ortho*-substituted dimethylanilines.[11] The ultraviolet absorption spectrum of the unsaturated amine closely resembled that of *o*-vinyldimethylaniline which is entirely different from the spectra of dimethylanilines with large saturated *ortho*-alkyl groups.[12] There is thus little doubt that the constitution of the methine base is *o-cyclo*hex-1-enyl-*NN*-dimethylaniline (IV). This result has recently been confirmed by Masamune.[13]

The product (IV) failed to undergo dehydrogenation to 2-dimethylaminodiphenyl with either palladium–charcoal or chloranil. On the other hand, hydrogenation in acetic acid over a platinum catalyst gave 1-dimethylamino-2-*cyclo*hexyl*cyclo*hexane (VII). In view of the reduction conditions, the product is assumed to have the *cis*-configuration while the isomer prepared by hydrogenation at high temperature and pressure over Raney nickel is regarded as the *trans*-compound (VIII). The reduction products (VII) and (VIII) were independently synthesised from 2-*cyclo*hexyl*cyclo*hexanone oxime[14] (IX). Thus, hydrogenation of the oxime using Adams catalyst in acetic acid and methylation of the resulting primary amine gave a 1-dimethylamino-2-*cyclo*hexyl*cyclo*hexane, identical



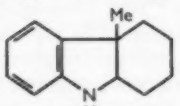
(IX)



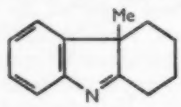
(X)

with the base (VII) which on the basis of the Auwers–Skita rule, confirmed in this case by the application of conformational analysis, is the *cis*-isomer. When the oxime was reduced with sodium and ethanol the methylated product was the *trans*-compound identical with (VIII).

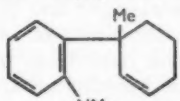
Examination of a model of one of the feasible structures for *cis*-hexahydro-9-methylcarbazole methohydroxide (X) (cf. conformation of *cis*-octahydro-1-methylindole methohydroxide, Part IV) shows that the necessary conformational requirement for easy Hofmann fission is satisfied by elimination of either the axial 1-hydrogen atom or the hydrogen atom attached to $C_{(11)}$. Thus, in the exhaustive methylation, formation of base (IV) can occur either by elimination of a β-proton from $C_{(11)}$ or, alternatively, elimination from $C_{(1)}$ and subsequent shift of the double bond into conjugation. Elimination



(XI)



(XII)



(XIII)

from $C_{(11)}$ is favoured on electronic grounds, since the hydrogen atom at $C_{(11)}$ is very acidic owing to the adjacent aromatic residue. Moreover, Weinstock and Bordwell[15] have shown that 3-phenyl*cyclo*hexene does not rearrange to 1-phenyl*cyclo*hexene under the conditions of a Hofmann elimination. It is therefore likely that the degradation proceeds by direct elimination of a proton from position 11. However, it was of interest to discover whether, for any reason, elimination from $C_{(1)}$ was impossible. For this purpose, the

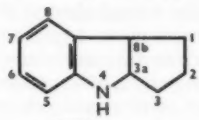
[11] Fahim and Fleifel, *J.*, 1951, 2761; Evans, Watson, and Williams, *J.*, 1939, 1348.
[12] Remington, *J. Amer. Chem. Soc.*, 1945, **67**, 1838.
[13] Masamune, *Bull. Chem. Soc. Japan*, 1957, **30**, 491.
[14] Hückel and Doll, *Annalen*, 1936, **526**, 103.
[15] Weinstock and Bordwell, *J. Amer. Chem. Soc.*, 1955, **77**, 6706.

XUM

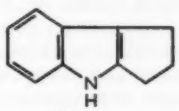
exhaustive methylation of *cis*-1 : 2 : 3 : 4 : 10 : 11-hexahydro-11-methylcarbazole (XI) was examined.

The base (XI) has been prepared by reducing tetrahydro-11-methylcarbazolenine (XII) with tin and hydrochloric acid.[16] This preparation was successfully repeated but the product was more conveniently prepared by reduction with sodium and ethanol; no indication of the presence of an isomer was obtained. Decomposition of *cis*-hexahydro-9 : 11-dimethylcarbazole methohydroxide at 115—120° gave a mixture consisting of an unsaturated base, presumably *NN*-dimethyl-*o*-(1-methyl*cyclo*hex-2-enyl)aniline (XIII), and 6—7% of hexahydro-9 : 11-dimethylcarbazole. The unsaturated base was even more inert to methyl iodide than was the methine (IV) derived from hexahydrocarbazole, being unchanged by methyl iodide for 6 hours at 100° in a sealed tube.

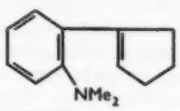
cis-1 : 2 : 3 : 3a : 4 : 8b-Hexahydro*cyclo*pent[*b*]indole (XIV) was first prepared by Plant and Rippon[17] by reduction of tetrahydro*cyclo*pent[*b*]indole (XV) electrolytically in acid solution. In the present investigation, the tetrahydro-compound was hydrogenated in dioxan over Raney nickel at 70—75° and 75 atmospheres' pressure,[18] theyield of base (XIV) being almost theoretical in remarkable contrast to the hydrogenation of tetrahydrocarbazole (see above). Reduction of tetrahydro*cyclo*pent[*b*]indole with tin and hydrochloric acid gave no hexahydro-compound, possibly owing to rapid oxidation of the unstable tetrahydro-compound[19] under these conditions. Ring scission of hexahydro-



(XIV)



(XV)



(XVI)

*cyclo*pent[*b*]indole occurred extremely readily, decomposition of the methohydroxide beginning at 35—45° and becoming vigorous at 80—100°. Formulation of the product as *NN*-dimethyl-*o*-*cyclo*pent-1-enylaniline (XVI) is based on ultraviolet absorption measurements which reveal the conjugated system as with the corresponding product from hexahydro-9-methylcarbazole methohydroxide, and on the profound change in the spectrum which follows reduction to *NN*-dimethyl-*o*-*cyclo*pentylaniline.

Experimental

2 : 3-*Dihydro*-1 : 1-*dimethylindolium Iodide*.—2 : 3-Dihydroindole[20] (7 g.) was converted by the usual procedure into 2 : 3-dihydro-1 : 1-dimethylindolium iodide (14 g., 87%). Crystallisation from ethanol gave colourless plates, m. p. 196—197° (decomp.) (von Braun and Neumann[21] give m. p. 195—196°). The *picrate* crystallised from aqueous methanol in yellow needles, m. p. 120—121° (Found: C, 51·0; H, 4·3; N, 14·7. $C_{14}H_{16}O_7N_4$ requires C, 51·1; H, 4·3; N, 14·9%).

Exhaustive Methylation of **2 : 3-*Dihydroindole*** (with K. G. Mason).—The above methiodide (13·5 g.) was dissolved in water (125 c.c.) and shaken in the dark with silver oxide, freshly prepared from silver nitrate (13 g.) and sodium hydroxide (4·2 g.). When a sample of the filtered solution gave a negative test for iodide ions, the mixture was filtered and the filtrate evaporated under reduced pressure at 45—50°. When most of the water had been removed, the temperature was raised to 130°. The syrupy quaternary hydroxide decomposed at 80—110° yielding a distillate of *o*-dimethylaminostyrene (5·1 g., 71%), b. p. 101°/25 mm. (Seeley, Yates, and Noller[22] record b. p. 78—80°/3 mm.), n_D^{25} 1·5602 (Found: C, 81·5; H, 8·6; N, 9·3. Calc.

[16] Plancher, Cecchetti, and Ghigi, *Gazetta*, 1929, **59**, 334.
[17] Plant and Rippon, *J.*, 1928, 1906.
[18] Cf. Heseltine and Brooker, U.S.P. 2,636,035/1953.
[19] Cf. Witkop and Patrick, *J. Amer. Chem. Soc.*, 1951, **73**, 2196; Witkop, Patrick, and Rosenblum, *ibid.*, p. 2641.
[20] Barltrop, King, and Walley, *J.*, 1945, 277.
[21] von Braun and Neumann, *Ber.*, 1916, **49**, 1283.
[22] Seeley, Yates, and Noller, *J. Amer. Chem. Soc.*, 1951, **73**, 772.

for $C_{10}H_{13}N$: C, 81·6; H, 8·9; N, 9·5%), $\lambda_{max.}$ 202, 234, 257 (infl.), and 309 mμ (ε 15,340, 16,990, 8860, and 2380 respectively in EtOH). The base gave the *picrate* (from ethanol), prisms, m. p. 116—117° (Found: C, 50·9; H, 4·1; N, 14·9. $C_{16}H_{16}O_7N_4$ requires C, 51·1; H, 4·3; N, 14·9%), *picrolonate*, needles, m. p. 158° (decomp.) (from ethanol) (Found: C, 58·3; H, 5·2; N, 17·0. $C_{20}H_{21}O_5N_5$ requires C, 58·4; H, 5·1; N, 17·0%), and *methiodide*, plates (from methanol), m. p. 186—187° (decomp.) (Found: C, 45·5; H, 5·4. $C_{11}H_{16}NI$ requires C, 45·7; H, 5·6%).

o-*Ethyl*-NN-*dimethylaniline*.—*o*-Dimethylaminostyrene (3·85 g.) was hydrogenated in the form of its hydrochloride in methanol over palladised charcoal at room temperature and pressure. After filtration the solution was evaporated and the residue treated with aqueous alkali and extracted with ether. *o*-Ethyl-*NN*-dimethylaniline (2·1 g., 54%) was thus obtained as an oil, b. p. 81·5—82°/14 mm. (von Braun and Neumann [21] record b. p. 87—88°/19 mm.), n_D^{21} 1·5177 (Found: C, 80·7; H, 10·0; N, 9·3. Calc. for $C_{10}H_{15}N$: C, 80·5; H, 10·1; N, 9·4%), $\lambda_{max.}$ 208 and 247 mμ (ε 14,210 and 4780 respectively in EtOH) (cf. *o*-methyl-*NN*-dimethylaniline [12]). It gave a picrate (from ethanol), long prisms, m. p. 149—150° (von Braun and Neumann,[21] m. p. 145°) (Found: C, 50·5; H, 4·9; N, 14·7. Calc. for $C_{16}H_{18}O_7N_4$: C, 50·8; H, 4·8; N, 14·8%), *picrolonate* (from ethanol), prisms, m. p. 165° (decomp.) (Found: C, 58·0; H, 5·5; N, 16·6. $C_{20}H_{23}O_5N_5$ requires C, 58·1; H, 5·6; N, 16·9%), and *hydriodide* (from acetone–ethyl acetate), plates, m. p. 154—155° (Found: C, 43·3; H, 5·7. $C_{10}H_{16}NI$ requires C, 43·3; H, 5·8%). The *methiodide*, m. p. 196—197°, was formed very slowly from the base and methyl iodide (von Braun and Neumann [21] record m. p. 162—164°) (Found: C, 45·1; H, 6·2. $C_{11}H_{18}NI$ requires C, 45·4; H, 6·2%).

2 : 3-*Dihydro*-1 : 1 : 2-*trimethylindolium Iodide*.—2 : 3-Dihydro-2-methylindole [23] (4·5 g.) was heated on a water-bath with methyl iodide (11 g.) and aqueous sodium hydroxide (1·4 g. in 15 c.c. of water). After 2 hr., the solution was cooled and extracted with chloroform. The dried ($MgSO_4$) extracts were concentrated and then poured into ether, the methiodide (8·5 g., 86%) being precipitated. Crystallisation from methanol–ethyl acetate gave colourless prisms, m. p. 208—210° (Bamberger and Sternitzki [3] record m. p. 211°; von Braun, Heider, and Neumann [4] record m. p. 202°; Adkins and Coonradt [7] record m. p. 208—210°) (Found: C, 45·9; H, 5·3. Calc. for $C_{11}H_{16}NI$: C, 45·7; H, 5·5%).

2 : 3-*Dihydro*-1 : 2-*dimethylindole*.—The above methiodide (8 g.) was dissolved in water and treated with silver chloride, freshly prepared from silver nitrate (12 g.). The mixture was kept overnight, then filtered and evaporated under reduced pressure at 40—50°. When most of the water had been removed, the syrupy residue was decomposed by heating it at 220°. Extraction of the distillate with ether yielded 2 : 3-*dihydro*-1 : 2-*dimethylindole* (2·9 g., 71%), b. p. 100—105° (bath-temp.)/25 mm., n_D^{18} 1·5505 (Found: C, 81·5; H, 8·7. $C_{10}H_{13}N$ requires C, 81·6; H, 8·8%). The *picrate* crystallised from ethanol in plates, m. p. 128—130° (Found: C, 50·8; H, 4·3. $C_{16}H_{16}O_7N_4$ requires C, 51·1; H, 4·3%). The *picrolonate* crystallised from ethanol in prisms, m. p. 167—168° (Found: C, 58·5; H, 5·2. $C_{20}H_{21}O_5N_5$ requires C, 58·4; H, 5·1%). The methiodide, prepared by refluxing an ethereal solution of the base with methyl iodide for 15 hr., had m. p. and mixed m. p. 208—210°.

Exhaustive Methylation of 2 : 3-*Dihydro*-2-*methylindole*.—This was carried out as described for 2 : 3-dihydroindole. The methohydroxide from 2 : 3-dihydro-1 : 1 : 2-trimethylindolinium iodide (6·5 g.) decomposed at 70°, yielding NN-*dimethyl*-o-*propenylaniline* (2·8 g., 77%), b. p. 95—98° (bath-temp.)/15 mm., n_D^{19} 1·5556 (Found: C, 81·8; H, 9·2. $C_{11}H_{15}N$ requires C, 82·1; H, 9·3%), $\lambda_{max.}$ 202, 233, and 303 mμ (ε 16,130, 15,880, and 2136 respectively in EtOH). The base gave a *picrate*, prisms, m. p. 168—170° (from ethanol) (von Braun *et al.*[4] record m. p. 158° for the picrate of the exhaustive methylation product) (Found: C, 52·5; H, 4·8. $C_{17}H_{18}O_7N_4$ requires C, 52·3; H, 4·6%), and a *picrolonate*, leaflets, m. p. 165—166° (from ethanol) (Found: C, 59·5; H, 5·7. $C_{21}H_{23}O_5N_5$ requires C, 59·3; H, 5·4%).

NN-*Dimethyl*-o-n-*propylaniline*.—*NN*-Dimethyl-*o*-propenylaniline (1·3 g.) was hydrogenated in ethanol (20 c.c.) over palladised charcoal at room temperature and pressure (1·15 mol. absorbed). After filtration, the solution was evaporated and distilled, giving NN-*dimethyl*-o-n-*propylaniline* (1·1 g.), b. p. 87—90° (bath-temp.)/15 mm., n_D^{16} 1·5137 (Found: C, 81·2; H, 10·5. $C_{11}H_{17}N$ requires C, 81·0; H, 10·4%), $\lambda_{max.}$ 208 and 248 mμ (ε 13,640 and 4690 respectively in EtOH). The *picrate* crystallised from ethanol in prisms, m. p. 176—178° (Found: C, 52·2; H, 5·1. $C_{17}H_{20}O_7N_4$ requires C, 51·2; H, 5·1%), and the *picrolonate* in rods, m. p. 136—138° (Found: C, 58·8; H, 5·5. $C_{21}H_{25}O_5N_5$ requires C, 59·1; H, 5·85%).

[23] Clarke and Pope, *J.*, 1904. **85**. 1331.

Catalytic Reduction of 1 : 2 : 3 : 4-*Tetrahydrocarbazole*.—The following indicates the standard procedure when using Raney nickel. Tetrahydrocarbazole (20 g.) in methanol (50 c.c.) was hydrogenated at an initial pressure of 120 atm.; and after removal of the catalyst and solvent, the product was treated with ether and dilute hydrochloric acid. Evaporation of the ethereal solution gave tetrahydrocarbazole, m. p. 118—119°, and when the acid extract was basified 1 : 2 : 3 : 4 : 10 : 11-hexahydrocarbazole, m. p. 98—99°, was precipitated. If the reaction time exceeded 10 hr. basification of the acidic extracts produced an uncrystallisable oil, which was not further investigated.

1 : 2 : 3 : 4-*Tetrahydro*-9-*methylcarbazole and its Catalytic Reduction*.—Tetrahydrocarbazole (45 g.) was methylated by the procedure used by Gilman and Spatz [24] for carbazole. The tertiary base (37 g., 76%) crystallised from methanol in plates, m. p. 49—50° (Perkin and Plant [25] record m. p. 50°).

The reduction procedure used was similar to that indicated for tetrahydrocarbazole. The products were *cis*-1 : 2 : 3 : 4 : 10 : 11-hexahydro-9-methylcarbazole, m. p. 50—51° (Gurney and Plant [26] record m. p. 50°), and unchanged tetrahydro-compound, m. p. 49—50°.

cis-1 : 2 : 3 : 4 : 10 : 11-*Hexahydro*-9-*methylcarbazole* (cf. Stevens and Tucker [27]).—*cis*-Hexahydrocarbazole (1·7 g.) was dissolved in a mixture of acetone (10 c.c.) and 66% potassium hydroxide solution (10 c.c.). Dimethyl sulphate (5 g.) was added in 10 portions, with shaking, during 15 min. The mixture was then shaken for a further 30 min., then poured into water. Isolation by ether-extraction yielded *cis*-hexahydro-9-methylcarbazole (0·6 g.), b. p. 140—145° (bath-temp.)/12 mm. (Perkin and Plant [5] and von Braun and Schörnig [28] give b. p. 144°/15 mm.). The picrate formed leaflets, m. p. 145—146° [Perkin and Plant [5] give m. p. 143—144° (decomp.)] (Found: C, 54·8; H, 4·8; N, 13·5. Calc. for $C_{19}H_{20}O_7N_4$: C, 54·7; H, 4·6; N, 13·5%). The methiodide crystallised from ethanol in square prisms, m. p. and mixed m. p. with a sample prepared by the method of von Braun *et al.*,[4] 192—193° (von Braun *et al.* record m. p. 187°) (Found: C, 51·1; H, 6·1; N, 4·3. Calc. for $C_{14}H_{20}NI$: C, 51·2; H, 6·3; N, 4·3%). The *methopicrate* crystallised from ethanol in needles, m. p. 168—170° (Found: C, 56·1; H, 5·1. $C_{20}H_{22}O_7N_4$ requires C, 55·8; H, 5·1%).

Exhaustive Methylation of cis-1 : 2 : 3 : 4 : 10 : 11-*Hexahydrocarbazole*.—This was carried out as described for 2 : 3-dihydroindole. The methohydroxide from *cis*-1 : 2 : 3 : 4 : 10 : 11-hexahydro-9-methylcarbazole methiodide [4] (42 g., m. p. 192—193°) was decomposed at 85—90°, yielding o-cyclo*hex*-1-*enyl*-NN-*dimethylaniline* (20·1 g., 78%), b. p. 141—142°/14 mm., 275°/767 mm. (Siwoloboff), n_D^{21} 1·5605 (Found: C, 83·7; H, 9·1; N, 6·9. $C_{14}H_{19}N$ requires C, 83·6; H, 9·5; N, 7·0%), $\lambda_{max.}$ 210, 226, and 260 mμ (ε 11,300, 14,400, and 5600 respectively in EtOH). The base afforded a *picrate* (from ethanol), leaflets, m. p. 164—166° (decomp.) (Found: C, 55·7; H, 5·4; N, 13·1. $C_{20}H_{22}O_7N_4$ requires C, 55·8; H, 5·1; N, 13·0%), *methiodide* (formed very slowly), needles (from acetone), m. p. 171—172° (Found: C, 52·8; H, 6·5. $C_{15}H_{22}NI$ requires C, 52·5; H, 6·4%), and *methopicrate*, plates (from ethanol), m. p. 168·5—169·5° (Found: C, 57·1; H, 5·4. $C_{21}H_{24}O_7N_4$ requires C, 56·8; H, 5·4%).

o-cyclo*Hexyl*-NN-*dimethylaniline*.—*o-cyclo*Hex-1-enyl-*NN*-dimethylaniline (4 g.) was hydrogenated in ethanol (45 c.c.) over 5% palladised charcoal (2 g.) during 12 hr. at room temperature. Working up in the usual way gave o-cyclo*hexyl*-NN-*dimethylaniline* (3·1 g., 75%), b. p. 145—148° (bath-temp.)/15 mm., n_D^{22} 1·5256 (Found: C, 82·9; H, 10·6. $C_{14}H_{21}N$ requires C, 82·8; H, 10·4%), $\lambda_{max.}$ 209 mμ (ε 9350). The *picrate* crystallised from ethanol in leaflets, m. p. 162—164° (Found: C, 55·6; H, 5·6; N, 13·1. $C_{20}H_{24}O_7N_4$ requires C, 55·6; H, 5·6; N, 13·0%). A mixed m. p. with *o-cyclo*hex-1-enyl-*NN*-dimethylaniline picrate was at 141—152°.

cis-1-*Dimethylamino*-2-cyclo*hexyl*cyclo*hexane*.—The above base (1 g.) was hydrogenated in glacial acetic acid (25 c.c.) over Adams catalyst (300 mg.) at 70° and normal pressure (3·3 mols. absorbed in 12 hr.). After filtration, the liquid was evaporated under reduced pressure to remove acetic acid and then basified. Extraction with ether yielded cis-1-*dimethylamino*-2-cyclo*hexyl*cyclo*hexane*, b. p. 145—148° (bath-temp.)/12 mm., n_D^{18} 1·4964 (Found: C, 80·5; H, 12·9. $C_{14}H_{27}N$ requires C, 80·3; H, 13·0%). The *picrate* crystallised from ethanol as

[24] Gilman and Spatz, *J. Org. Chem.*, 1952, **17**, 860.
[25] Perkin and Plant, *J.*, 1921, 1825.
[26] Gurney and Plant, *J.*, 1927, 1318.
[27] Stevens and Tucker, *J.*, 1923, 2140.
[28] von Braun and Schörnig, *Ber.*, 1925, **58**, 2156.

XUM

needles, m. p. and mixed m. p. (see below) 110—111° (Found: C, 55·1; H, 6·5. $C_{20}H_{30}O_7N_4$ requires C, 54·8; H, 6·8%).

trans-1-*Dimethylamino*-2-cyclo*hexyl*cyclo*hexane*.—*o-cyclo*Hex-1-enyl-*NN*-dimethylaniline (2 g.) was hydrogenated in methanol (30 c.c.) over Raney nickel at 200—220°/180 atm. for 20 hr. After filtration, the solution was evaporated and the residue dissolved in ether. The basic material was extracted into dilute hydrochloric acid and recovered by basification and extraction with ether. 1-*Dimethylamino*-2-cyclo*hexyl*cyclo*hexane* (0·9 g.) was thus obtained as an oil, b. p. 150—154° (bath-temp.)/15 mm., n_D^{18} 1·4902 (Found: C, 80·5; H, 12·8%). The *picrate* crystallised from ethanol in needles, m. p. and mixed m. p. (see below), 167—168° (Found: C, 54·7; H, 6·8%).

2-*Dimethylaminodiphenyl*.—2-Aminodiphenyl was prepared from 2-nitrodiphenyl [29] by 6 hours' heating in ethanol with tin and concentrated hydrochloric acid (cf. Scarborough and Waters,[30] who used stannous chloride). The distilled base (5 g.) was methylated with dimethyl sulphate according to the method of Popkin, Perretta, and Selig.[31] The methylated bases were isolated by ether-extraction. After evaporation of the ethereal extracts, the residue was heated with acetic anhydride (15 c.c.) under reflux for 1 hr. The solution was cooled, then boiled with water (25 c.c.) for a few minutes to decompose excess of anhydride. Acetylated material was extracted into ether, and the tertiary base was recovered from the aqueous solution by basification and ether-extraction. This gave 2-dimethylaminodiphenyl (1·5 g., 26% based on the 2-aminodiphenyl), b. p. 146—148°/12 mm., n_D^{14} 1·6070 (Found: C, 85·3; H, 7·7. Calc. for $C_{14}H_{15}N$: C, 85·3; H, 7·6%) (Popkin *et al.*[31] record b. p. 118—120°/2·5 mm., n_D^{20} 1·6052—1·6058 and 1·6046—1·6050). The *picrate* crystallised from ethanol in prisms, m. p. 190—191° (decomp.) (Found: C, 56·3; H, 4·4. $C_{20}H_{18}O_7N_4$ requires C, 56·3; H, 4·2%). The *methiodide* (formed slowly) crystallised from acetone–ethyl acetate in prisms, m. p. 178—179° [Hey and Jackson [32] record m. p. 228° (decomp.)] (Found: C, 53·4; H, 5·4. $C_{15}H_{18}NI$ requires C, 53·1; H, 5·3%).

2-cyclo*Hexyl*cyclo*hexanone Oxime*.—2-*cyclo*Hexyl*cyclo*hexanone [33,34] (25 g.) with hydroxylamine hydrochloride (20 g.) and sodium hydroxide (11·5 g.) in aqueous ethanol formed the oxime (24 g., 89%), m. p. 99—102° (Wallach [33] records m. p. 100°; Hückel and Doll [14] give m. p. 101—102° and m. p. 103—104° for the isomeric oximes).

trans-2-cyclo*Hexyl*cyclo*hexylamine*.—The above oxime (6 g.) was reduced in refluxing ethanol (100 c.c.) by sodium (10 g.) added during 1½ hr. After acidification with dilute hydrochloric acid, the solution was concentrated to 25 c.c. and kept overnight at 0°. The base hydrochloride was filtered off at the pump, dissolved in water, and basified with excess of aqueous ammonia. trans-2-cyclo*Hexyl*cyclo*hexylamine*, recovered by extraction with ether, had b. p. 145—148° (bath-temp.)/11 mm., n_D^{17} 1·4970 (Found: C, 79·4; H, 12·2; N, 7·9. $C_{12}H_{23}N$ requires C, 79·6; H, 12·7; N, 7·8%). The benzoyl derivative crystallised from aqueous ethanol in needles, m. p. 157—158° (Hückel and Doll [14] record m. p. 157—158°). The *hydrochloride* crystallised from acetone–ether in hexagonal plates, m. p. 215—216° (Found: C, 66·2; H, 11·2. $C_{12}H_{24}NCl$ requires C, 66·2; H, 11·0%).

trans-1-*Dimethylamino*-2-cyclo*hexyl*cyclo*hexane*.—*trans*-2-cyclo*Hexyl*cyclo*hexylamine* (1 g.), 40% aqueous formaldehyde (1·5 c.c.), and 95% formic acid (1 g.) were heated on a water-bath for 5 hr. The tertiary base (0·7 g.) was isolated by ether-extraction of the basified solution and had b. p. 140—145° (bath-temp.)/10 mm., n_D^{18} 1·4893 (Found: C, 80·6; H, 12·5%). The picrate crystallised from ethanol in needles, m. p. 167—168°.

cis-2-cyclo*Hexyl*cyclo*hexylamine*.—2-*cyclo*Hexyl*cyclo*hexanone oxime (4 g.) was hydrogenated in glacial acetic acid (30 c.c.) over Adams catalyst (150 mg.) at room temperature and pressure. Absorption of hydrogen was slow and the catalyst was added in 3 portions of 50 mg. each at intervals of 24 hr. After filtration, the solution was heated to remove acetic acid, and the crude amine was isolated by ether-extraction of the basified solution. Dry hydrogen chloride was bubbled through the ethereal solution, cis-2-cyclo*hexyl*cyclo*hexylamine hydrochloride* (3·5 g., 78%) being precipitated. Crystallisation from acetone–ether gave needles, m. p.

[29] Bell, Kenyon, and Robinson, *J.*, 1926, 1239.
[30] Scarborough and Waters, *J.*, 1927, 89.
[31] Popkin, Perretta, and Selig, *J. Amer. Chem. Soc.*, 1944, **66**, 833.
[32] Hey and Jackson, *J.*, 1934, 645.
[33] Wallach, *Annalen*, 1911, **381**, 95.
[34] Rapson, *J.*, 1941, 15.

XUM

166—168° (Found: C, 65·9; H, 11·0%). The hydrochloride was converted in the usual way into the base, b. p. 138—141° (bath-temp.)/12 mm., n_D^{19} 1·4976 (not analysed owing to rapid carbonate formation). The *benzoyl derivative* crystallised from ethanol in plates, m. p. 136—137° (Found: C, 79·7; H, 9·3. $C_{19}H_{27}ON$ requires C, 80·0; H, 9·5%).

cis-1-*Dimethylamino*-2-cyclo*hexyl*cyclo*hexane*.—The above primary base (0·6 g.), methylated as was its *trans*-isomer, gave the tertiary *base*, b. p. 144—148° (bath-temp.)/10 mm., n_D^{20} 1·4960 (Found: C, 80·6; H, 12·8%). The picrate crystallised from ethanol in needles, m. p. 110—111°.

cis-1 : 2 : 3 : 4 : 10 : 11-*Hexahydro*-11-*methylcarbazole*.—(i) (cf. Plancher, Cecchetti, and Ghigi [16]) 1 : 2 : 3 : 4-Tetrahydro-11-methylcarbazolenine [35] (65 g.), ethanol (120 c.c.), concentrated hydrochloric acid (260 c.c.), and granulated tin (130 g.) were heated under reflux on a water-bath for 5 hr. After filtration through glass wool, the hot mixture was allowed to cool; the base chlorostannate crystallised and was filtered off at the pump. After decomposition of the chlorostannate with 40% sodium hydroxide solution (600 c.c.) and repeated ether-extraction, the base was obtained as an oil (40 g.), b. p. 144—146°/14 mm. An attempt to purify it through the hydrochloride, m. p. 217—220° (Plancher *et al.*[16] record m. p. 220°), failed owing to the decomposition of the hydrochloride. The base (40 g.) was heated under reflux with acetic anhydride (100 c.c.) for 1 hr. The solution was basified and ether-extracted, yielding cis-9-*acetyl*-1 : 2 : 3 : 4 : 10 : 11-*hexahydro*-11-*methylcarbazole*. Crystallisation from ethanol gave colourless prisms (39 g.), m. p. 87—88° (Found: C, 78·7; H, 8·6. $C_{15}H_{19}ON$ requires C, 78·6; H, 8·3%). The recrystallised acetyl compound was hydrolysed with boiling 10% sodium hydroxide solution (200 c.c.) for 2 hr. Extraction with ether then gave pure *cis*-1 : 2 : 3 : 4 : 10 : 11-hexahydro-11-methylcarbazole (27·5 g., 42%), b. p. 144—146°/14 mm., n_D^{17} 1·5700 (Found: C, 83·6; H, 9·3. Calc. for $C_{13}H_{17}N$: C, 83·4; H, 9·1%). The *benzoyl derivative* crystallised from aqueous ethanol or ethyl acetate in prisms, m. p. 96—97° (Found: C, 82·4; H, 7·4. $C_{20}H_{21}ON$ requires C, 82·5; H, 7·2%).

(ii) 1 : 2 : 3 : 4-Tetrahydro-11-methylcarbazolenine (8 g.), in ethanol (350 c.c.), was gently boiled under reflux while sodium (30 g.) was added during 1½ hr. The cooled solution was acidified with dilute hydrochloric acid and then heated under reduced pressure to remove ethanol. Basification with ammonia and ether-extraction gave 1 : 2 : 3 : 4 : 10 : 11-hexahydro-11-methylcarbazole (7·3 g., 90%), b. p. 140—143°/10 mm., n_D^{17} 1·5700. The acetyl derivative, prepared in 96% yield, had m. p. and mixed m. p. with the acetyl compound prepared as above, 86·5—88°.

cis-1 : 2 : 3 : 4 : 10 : 11-*Hexahydro*-9 : 11-*dimethylcarbazole*.—Dimethyl sulphate (5 c.c.) was added dropwise to a stirred mixture of hexahydro-11-methylcarbazole (1 g.), acetone (10 c.c.), and 66% potassium hydroxide solution (10 c.c.). Then the mixture was stirred for 1 hr. and poured into water (10 c.c.). Extraction with ether yielded cis-1 : 2 : 3 : 4 : 10 : 11-*hexahydro*-9 : 11-*dimethylcarbazole* (0·4 g.), b. p. 145—149° (bath-temp.)/10 mm., n_D^{19} 1·5049 (Found: C, 83·3; H, 9·4. $C_{14}H_{19}N$ requires C, 83·6; H, 9·5%). The *methiodide*, prepared by refluxing the base and methyl iodide in ether for 20 hr., crystallised from acetone–ethyl acetate in prisms, m. p. 192—193° (Found: C, 52·4; H, 6·3. $C_{15}H_{22}NI$ requires C, 52·5; H, 6·4%). The *methopicrate* crystallised from ethanol in orange prisms, m. p. 155—156° (Found: C, 56·1; H, 4·9. $C_{21}H_{24}O_7N_4$ requires C, 56·1; H, 4·7%).

cis-1 : 2 : 3 : 4 : 10 : 11-*Hexahydro*-9 : 9 : 11-*trimethylcarbazolium Iodide*.—This compound was most conveniently prepared from hexahydro-11-methylcarbazole (27·5 g.), acetone (50 c.c.), 40% potassium hydroxide solution (21 c.c.), and excess of methyl iodide heated under reflux for 12 hr. After evaporation to remove methyl iodide and acetone, the mixture was cooled and filtered. Recrystallisation of the solid from water or ethanol–ether gave the pure methiodide (30 g., 59%) as prisms, m. p. and mixed m. p. with a sample prepared from the tertiary base, 192—193°.

Exhaustive Methylation of cis-1 : 2 : 3 : 4 : 10 : 11-*Hexahydro*-11-*methylcarbazole*.—This was carried out as described for 2 : 3-dihydroindole. The methohydroxide from the above methiodide (18 g.) decomposed at 115—120°. When the temperature was raised further, the product distilled as an oil (11·3 g.), b. p. 138—140°/14 mm. The oil (1·2 g.) was heated with excess of methyl iodide under reflux for 3 days. After evaporation, dry ether was added and the precipitated solid (0·13 g.) was removed. Crystallisation from ethanol–ether gave colourless prisms of 1 : 2 : 3 : 4 : 10 : 11-hexahydro-9 : 9 : 11-trimethylcarbazolium iodide, m. p. and

[35] Pausacker, *J.*, 1950, 621.

XUM

mixed m. p. 190—192°. Evaporation of the ethereal filtrate gave an oil (1 g.) which was converted into the picrate. Crystallisation from aqueous ethanol gave NN-*dimethyl*-o-(1-*methyl*cyclo*hex*-2-*enyl*)*aniline picrate* as yellow needles, m. p. 124—125° (Found: C, 56·7; H, 5·5; N, 12·2. $C_{21}H_{24}O_7N_4$ requires C, 56·8; H, 5·4; N, 12·6%). Decomposition of the picrate with 10% lithium hydroxide solution, followed by extraction with ether, gave the *base*, b. p. 139—140°/14 mm., n_D^{20} 1·5400 (Found: C, 83·4; H, 9·6. $C_{18}H_{21}N$ requires C, 83·7; H, 9·8%), $\lambda_{max.}$ 209 mμ (ε 11,430 in EtOH).

NN-*Dimethyl*-o-(1-*methyl*cyclo*hexyl*)*aniline*.—The above unsaturated base (1·2 g.) was completely hydrogenated in 6 hr. in ethanol (10 c.c.) over palladised charcoal at room temperature and pressure. Isolation in the usual way gave NN-*dimethyl*-o-(1-*methyl*cyclo*hexyl*)-*aniline*, b. p. 135—140° (bath-temp.)/12 mm., n_D^{16} 1·5331 (Found: C, 82·8; H, 10·5. $C_{15}H_{23}N$ requires C, 83·0; H, 10·6%), $\lambda_{max.}$ 210 mμ (ε 9485 in EtOH). The *picrate* crystallised from aqueous ethanol in prisms, m. p. 160—161° (Found: C, 56·8; H, 5·8. $C_{21}H_{26}O_7N_4$ requires C, 56·7; H, 5·8%).

cis - 1 : 2 : 3 : 3*a* : 4 : 8*b* - *Hexahydro*cyclo*pent*[b]*indole* (Heseltine and Brooker [18]) 1 : 2 : 3 : 4-Tetrahydro*cyclo*pent[*b*]indole [16] (21 g.) in dioxan (80 c.c.) was reduced for 24 hr. at 70—75° with hydrogen at an initial pressure of 75 atm. and in the presence of Raney nickel. The mixture was filtered and evaporated under reduced pressure to remove dioxan. The residue was dissolved in ether and extracted several times with dilute sulphuric acid. The crude base was recovered by ether-extraction of the basified extracts. *cis*-1 : 2 : 3 : 3a : 4 : 8b-Hexahydro*cyclo*pent[*b*]indole was thus isolated as an oil (20 g., 94%), b. p. 131—134°/13 mm. (Plant and Rippon [17] record b. p. 152°/16 mm; Heseltine and Brooker [18] give b. p. 98—100°/10 mm.). The picrate, acetyl derivative, and benzoyl derivative had m. p. 157—159°, 77—79°, and 86—87° respectively (Plant and Rippon [17] give m. p. 159°, 78°, and 86° respectively).

cis-1 : 2 : 3 : 3*a* : 4 : 8*b*-*Hexahydro*-4-*methyl*cyclo*pent*[b]*indole*.—Dimethyl sulphate (50 g.) was added dropwise during 1 hr. to a stirred mixture of the above base (20 g.), acetone (100 c.c.), and 10% sodium hydroxide solution (100 c.c.). The mixture was stirred for a further 30 min., evaporated to remove acetone, and then extracted several times with ether. Evaporation of the dried ethereal extracts yielded the crude tertiary base, which was heated under reflux with acetic anhydride (30 c.c.) for 30 min. The solution was evaporated under reduced pressure to remove excess of anhydride, treated with sodium hydrogen carbonate solution, and extracted with ether. The ethereal solution was shaken with dilute hydrochloric acid, and the tertiary base was recovered from the acid extract in the usual way. *cis*-1 : 2 : 3 : 3a : 4 : 8b-Hexahydro-4-methyl*cyclo*pent[*b*]indole was thus isolated as a colourless oil (6·2 g., 28%), b. p. 127—129°/10 mm., n_D^{17} 1·5668 (Found: C, 82·8; H, 8·8. Calc. for $C_{12}H_{15}N$: C, 83·2; H, 8·7%). The *picrate* crystallised from ethanol in yellow plates, m. p. 121—122° (Found: C, 54·0; H, 4·7. $C_{18}H_{18}O_7N_4$ requires C, 53·8; H, 4·5%) (Plant and Rippon [17] record b. p. 136—137°/15 mm., picrate, m. p. 116°).

The aqueous solution remaining after the first ether-extraction in the above procedure was treated with concentrated aqueous potassium iodide; the base methiodide was precipitated. Crystallisation from acetone gave *cis*-hexahydro-4 : 4-dimethyl*cyclo*pent[*b*]indolium iodide as prisms (23 g.), m. p. 187—189° (Found: C, 49·5; H, 5·7. Calc. for $C_{13}H_{18}NI$: C, 49·6; H, 5·8%) (Plant and Rippon [17] give m. p. 189°). The quaternary *picrate* crystallised from ethyl acetate–ethanol in elongated prisms, m. p. 133—134° (Found: C, 54·9; H, 4·9. $C_{19}H_{20}O_7N_4$ requires C, 54·8; H, 4·8%).

Exhaustive Methylation of cis-1 : 2 : 3 : 3*a* : 4 : 8*b*-*Hexahydro*cyclo*pent*[b]*indole*—This was carried out as described for 2 : 3-dihydroindole. Decomposition of the methohydroxide from 23 g. of methiodide commenced at 35—45° and was completed at 100—110°. Extraction with ether gave NN-*dimethyl*-o-cyclo*pent*-1-*enylaniline* (10·9 g., 80%), b. p. 125—126°/10 mm., n_D^{19} 1·5668 (Found: C, 83·4; H, 9·2. $C_{31}H_{17}N$ requires C, 83·4; H, 9·2%), $\lambda_{max.}$ 205, 231, and 301 mμ (ε 17,220, 16,210, and 1926 respectively in EtOH). The *picrate* crystallised from ethanol in plates, m. p. 152—153° (Found: C, 54·8; H, 4·9. $C_{19}H_{20}O_7N_4$ requires C, 54·8; H, 4·8%).

NN-*Dimethyl*-o-cyclo*pentylaniline*.—The exhaustive methylation product (3 g.) was hydrogenated in ethanol (50 c.c.) over 10% palladised charcoal (1 g.) at room temperature and

[16] Perkin and Plant, *J.*, 1923, **123**, 3242.

pressure, 1·1 mols. being absorbed in 1 hr. The solution was filtered, evaporated, and finally distilled, giving NN-*dimethyl*-o-cyclo*pentylaniline* (2·1 g., 69%), b. p. 123—124°/9 mm., n_D^{21} 1·5400 (Found: C, 82·2; H, 10·3. $C_{13}H_{19}N$ requires C, 82·5; H, 10·1%), $\lambda_{max.}$ 211 and 249 mμ (ε 13,790 and 4860 respectively in EtOH). The *picrate* crystallised from ethyl acetate–ethanol in elongated prisms, m. p. 133—134° (Found: C, 54·9; H, 4·9. $C_{19}H_{22}O_7N_4$ requires C, 54·5; H, 5·3%).

THE UNIVERSITY, NOTTINGHAM. [*Received, January 10th*, 1958.]

---

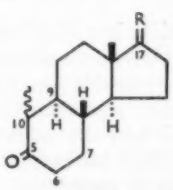
466. *Experiments on the Synthesis of Substances Related to the Sterols. Part LIV.* Degradative and Synthetical Studies on the A-Ring of Androst-4-ene-3 : 17-dione.*

By M. J. TEMPLE ROBINSON.

The A-ring of androst-4-ene-3 : 17-dione (III) has been degraded through the acid (V) to des-A-androstane-5 : 17-dione (I) (a structurally but not stereochemically identical racemic compound had been prepared previously [1]). By-products in the potassium permanganate oxidation of androst-4-ene-3 : 17-dione to the acid (V) and methods for reconverting this acid into the dione (III) have been studied.

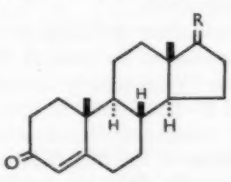
MARTIN and ROBINSON [1] obtained a mixture of stereoisomers of the diketone (I), which contains the B-, C-, and D-ring of androst-4-ene-3 : 17-dione (III), and isolated one racemate, m. p. 116—117°. An attempt to add the A-ring by condensing the diketone (I) with diethylmethyl-3-oxobutylammonium iodide gave derivatives of perhydro-1 : 2-benzofluorene [2] by reaction at position 16.† Because the overall yield of Martin and Robinson's diketone was low and the stereoisomerism of the five asymmetric centres was unknown the "natural" diketone (I) has been prepared as a potential relay by the degradation of androst-4-ene-3 : 17-dione.

The A-ring of some derivatives of cholest-4-en-3-one (IV) has been removed in one operation by oxidation, but the yields of the "Inhoffen ketone" (II) [3] were poor.[4] Further, it is now known [4] that $C_{(6)}$, as well as $C_{(16)}$, would be more reactive than $C_{(10)}$ in the diketone (I) and that the A-ring is best built up through acids such as (V) and (VI),[4] the



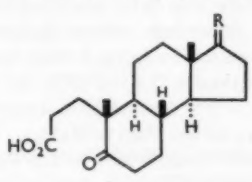
(I) : R = O

(II) : R =

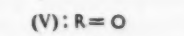


(III) : R = O

(IV) : R =



(V) : R = O

(VI) : R = 

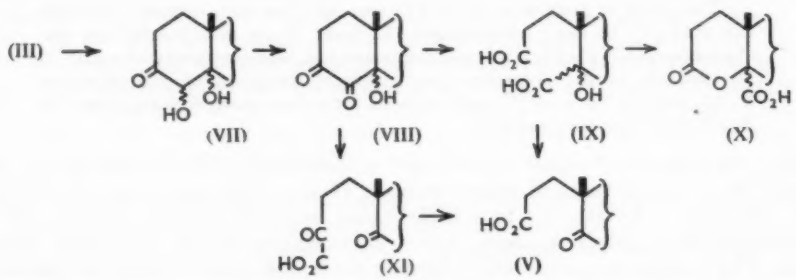
three carbon atoms being added at $C_{(10)}$ after the more reactive positions have been blocked.[4,5] For these reasons the A-ring of androst-4-ene-3 : 17-dione was removed stepwise so that the acid (V) could be used as a relay.

* Part LIII, Cornforth, Kauder, Pike, and Robinson, *J.*, 1955, 3348. † Steroid numbering.

[1] Martin and Robinson, *J.*, 1943, 491.
[2] *Idem*, *J.*, 1949, 1866.
[3] Inhoffen and Huang-Minlon, *Ber.*, 1938, **71**, 1720.
[4] Pinder and Robinson, *J.*, 1952, 1224.
[5] Woodward, Sondheimer, Taub, Heussler, and McLamore, *J. Amer. Chem. Soc.*, 1952, **74**, 4223.

XUM

The oxidation of androst-4-ene-3 : 17-dione (III) by potassium permanganate in acetone was studied in some detail in order to improve on yields previously obtained in similar oxidations (see, *e.g.*, Windaus [6]) and to elucidate the course of the reaction. At first this was greatly hindered by the practical difficulty of working with the poorly crystalline acid (V) and its oily methyl ester, but the ethyl ester was found to be very satisfactory. Derivatives of the acids (V) and (IX) (probably both isomers) were isolated when androst-4-ene-3 : 17-dione (III) was oxidised with the least amount of potassium permanganate required to convert it entirely into acidic compounds, but attempts to oxidise the acids (IX) to the keto-acid (V) by increasing the amount of oxidant merely increased the amount of intractable gums. Therefore, the acid (XI), though not isolated, may be the main intermediate leading to (V). The oxidation was completed by manganic acetate [7] prepared *in situ*, with care to avoid lactonising the acids (IX), and the acid (V) was converted directly into its ethyl ester in an overall yield of 50%. Lead tetra-acetate was unsuitable because the more abundant isomer of the acids (IX) formed an insoluble lead salt.



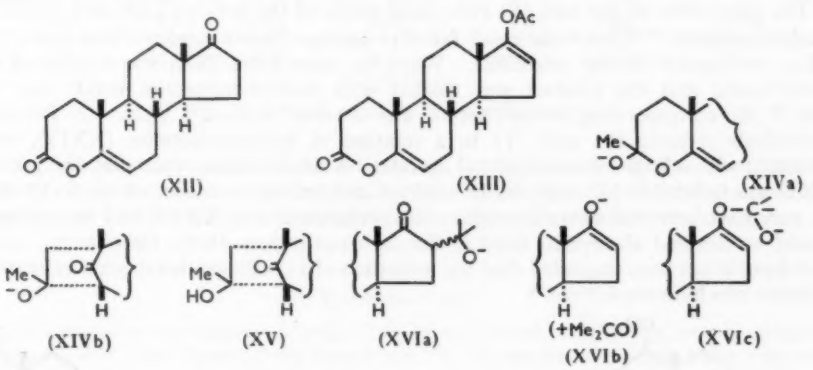
An alternative route to the acid (V) involved hydroxylation of androst-4-ene-3 : 17-dione (III) with osmium tetroxide and hydrogen peroxide [8] followed by oxidation of the diol (VII) (one isomer) with lead tetra-acetate in aqueous acetic acid.[9] Because the second reaction is very specific this method provided the first crystalline speciment of the acid (V) but the poor yield in the first stage made it impractical for larger preparations. Butenandt and Wolz [8] reported much better yields from analogous αβ-unsaturated ketones but the yields of the diol (VII) could not be improved.

The potassium permanganate oxidation provided several points of interest. The manganese oxides formed when the amount of the oxidant [less than the theoretical amount for oxidation to (IX) or (XI), let alone (V), if mainly manganese dioxide was formed] just sufficed to convert androst-4-ene-3 : 17-dione entirely into acidic products corresponded to $MnO_{1.7}$ rather than to MnO_2. The manganese dioxide which is formed as an intermediate presumably contributes to the oxidation of the diol (VII) to (VIII) (although manganese dioxide of a different quality and under different conditions is stated not to oxidise adipoin [10]) and possibly (VIII) to (IX) (cf. ref. 11). One isomer of the hydroxy-dibasic acids (IX) was isolated and its structure demonstrated by relating it and its dimethyl ester to one of the lactone acids (X) (cf. refs. 6, 12). The other isomer (IX) was only detected by isolating the methyl ester of the corresponding lactone acid (X), the structure of this ester being inferred from the close similarity of its infrared spectrum (particularly the carbonyl stretching frequencies) to that of its isomer.

[6] Windaus, *Ber.*, 1906, **39**, 2008.
[7] Criegee, Kraft, and Rank, *Annalen*, 1938, **507**, 159.
[8] Butenandt and Wolz, *Ber.*, 1938, **71**, 1483.
[9] Baer, Grosheintz, and Fischer, *J. Amer. Chem. Soc.*, 1939, **61**, 2607.
[10] Highet and Wildman, *ibid.*, 1955, **77**, 4399.
[11] Sondheimer, Amendolla, and Rosenkranz, *ibid.*, 1953, **75**, 5932.
[12] Tschesche, *Annalen*, 1932, **498**, 185.

Reconversion of the acid (V) into androst-4-ene-3 : 17-dione was more complicated than the analogous change for " Windaus acid " (VI). The methods used for the latter would have caused undesirable side reactions with the 17-carbonyl group which, therefore, had to be protected. Because the enol-lactone Grignard reaction has been so successful in related series [5,13] the enol-lactone enol-acetate (XIII) appeared to be suitable. If the addition of methylmagnesium iodide to an enol-lactone gives a stable intermediate such as (XIVa) the protection is readily understood. But the first products isolated in other cases [14] have structures such as (XV) formed by rearrangement of (XIVa) to (XIVb), the driving force coming from the lower energy of the system R–C–C=O than of the system C=C–O–R. Similar rearrangements account for the good yields of 1 : 3-diols obtained from Grignard reagents and some enol esters,[14] and it has been suggested that steric hindrance in the 10β-methyl series (the natural steroid series) prevents the 5-carbonyl group from reacting.[14] Successful protection at position 17 in the case of androst-4-ene-3 : 17-dione may, therefore, depend on the low reactivity of the hindered carbonyl group in (XVIa) rather than on the formation of the enol derivatives (XVIb) or (XVIc) as was first thought.

The sodium salt of the acid (V), which was more readily obtained pure than the acid itself by hydrolysis of the ethyl ester, was converted into the enol-lactone (XII) by boiling acetic anhydride. When the acid (V) was treated with acetic anhydride and acetyl chloride,[15] acetic anhydride and catalytic amounts of sodium acetate,[5] or *iso*propenyl acetate and an acid catalyst,[16] yields of the enol-lactone were low and variable, and excessive losses resulted when removing a neutral gummy by-product, probably containing the enol-acetate (XIII). The enol-lactone (XII) with *iso*propenyl acetate and toluene-*p*-



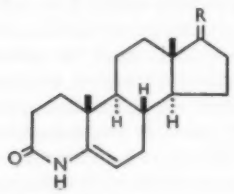
sulphonic acid gave the enol-acetate (XIII),[16] the acid being neutralised at the end of the reaction by filtering the reaction mixture through alumina. The enol-acetate was converted by methylmagnesium iodide followed by dilute alkali [13] into androst-4-ene-3 : 17-dione.

Because of the difficulties encountered during early preparations of the enol-lactone (XII) and the enol-acetate (XIII) other methods of protecting the carbonyl groups in the acid (V) by ketal formation or by reduction were tried but the following routes were unsuccessful:

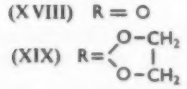
(*a*) The ethyl ester of the acid (V) with ethanolic ammonia at room temperature gave a substance thought to be the imino-lactam (XVII), probably contaminated with some of

[13] Fujimoto, *J. Amer. Chem. Soc.*, 1951, **73**, 1856.
[14] Zwahlen, Horton, and Fujimoto, *ibid.*, 1957, **79**, 3131.
[15] Turner, *ibid.*, 1950, **72**, 579.
[16] Moffett and Weisblat, *ibid.*, 1952, **74**, 2183.

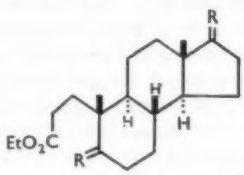
the ketone (XVIII) [the nitrogen analyses were low for (XVII)]. This gave a ketal (XIX) under the usual conditions for a ketone;[17] but when the ketal reacted with methylmagnesium iodide,[5,18] only basic tars were formed. (*b*) When benzylamine was used in the above series of reactions [5] no crystalline products were formed. (*c*) The ethyl ester of the acid (V) with ethyl orthoformate in acidified ethanol gave a substance which was not the expected bisdiethyl ketal (XX). Analytical and spectral data were later interpreted as



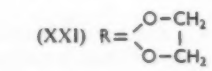
(XVII) R = NH
(XVIII) R = O



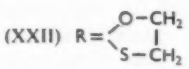
(XIX)



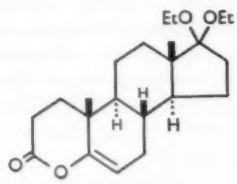
(XX)



(XXI)

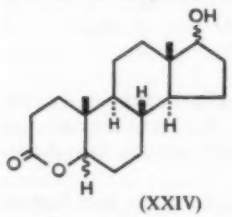


(XXII)

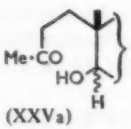


(XXIII)

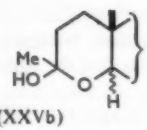
consistent with the structure (XXIII) but this conflicts with the strong positive optical rotation. It has been noted that ethyl γ-oxopimelate does not form a diethyl ketal.[19] (*d*) The ether ester of the acid (V) gave good yields of the ketals (XXI) and (XXII) by standard methods [17,20] but these ketals failed to undergo Claisen condensations in workable yields, even under forcing conditions. When the ester ketal (XX) was condensed with acetophenone and the product was treated with methylmagnesium iodide and then alkali [21] the corresponding methyl ketone was obtained in 1—2% yield. (*e*) Potassium borohydride reduced the acid (V) to a mixture of hydroxy-lactones (XXIV), which condensed with a large excess of phenyl acetate. A single isomer of the dihydroxy-ketone (XXV) was isolated but it could not be oxidised and cyclised to androst-4-ene-3 : 17-dione: this may have been due to the formation of a cyclic semiketal (XXVb) and this substance showed no infrared absorption band in the carbonyl region (1600—1800 cm.$^{-1}$); on the other hand it has been suggested that the formation of a cyclic semiketal can accelerate the oxidation of a hydroxy-ketone.[22]



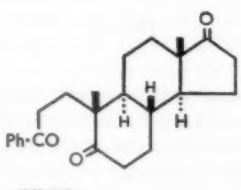
(XXIV)



(XXVa)



(XXVb)



(XXVI)

Experiments on the further degradation of the A-ring, in order to prepare the diketone (I), were based on the reported fission of several 1 : 5-dicarbonyl compounds.[23] The

[17] Poos, Arth, Beyler, and Sarett, *J. Amer. Chem. Soc.*, 1953, **75**, 422.
[18] McKenzie, Martin, and Rule, *J.*, 1914, **105**, 1583.
[19] Lukes, Poos, and Sarett, *J. Amer. Chem. Soc.*, 1952, **74**, 1401.
[20] Romo, Rosenkranz, and Djerassi, *ibid.*, 1951, **73**, 4961.
[21] Chaney and Astle, *J. Org. Chem.*, 1951, **16**, 57.
[22] Barton and Mayo, *J.*, 1956, 142.
[23] Achtermann, *Z. physiol. Chem.*, 1934, **225**, 141; Cornforth, Youhotsky, and Popják, *Nature*, 1954, **173**, 536; Riniker, Arigoni, and Jeger, *Helv. Chim. Acta*, 1954, **37**, 546.

XUM

phenyl ketone (XXVI) was prepared from the enol acetate (XIII) by the action of phenylmagnesium bromide. Heating this ketone or the ethyl ester of the acid (V) at *ca.* 300° for several hours, or boiling the ketone with potassium hydroxide in ethylene glycol, gave the diketone (I) in 1—2% yield. Fortunately at this stage of the work there appeared a correction to an earlier report [15] claiming that pyrolysis of the barium salt of the " Windaus acid " (VI) led to decarboxylation. It was found that the product was the " Inhoffen ketone " (II) formed by the loss of acrylic acid.[24] When the barium salt of the acid (V) was heated at 320—330°/0·01 mm. the diketone (I) was formed in 10—20% yield. This low yield may be due to the tendency of the *cyclo*pentanone ring in (I) to undergo base-catalysed condensations more readily than the *cyclo*hexanone ring,[2] so that more side reactions are likely in the pyrolysis of the acid (V) than of the " Windaus acid " (VI). No pure specimen of Martin and Robinson's synthetic (racemic) diketone, m. p. 116—117°,[1] was available for comparison with our product (I). When a very small impure specimen of the synthetic diketone was recrystallised from methanol a substance (B) of m. p. 130—131°, was obtained, a difference which may be due to polymorphism. The structural, but not stereochemical, identity of des-A-androst-5 : 17-dione (A) and the substance (B), m. p. 130—131°, may be inferred from the absorption bands observed in CCl_4 solution (see Table) and assigned to specific groups on the basis of R. N. Jones's empirical rules.[25] α-Methylene groups next to 4-, 6-, 7-, 11-, and 12-carbonyl groups and next to 3-carbonyl groups have been associated with bands at 1438—1426 and 1426—1415 cm.$^{-1}$ respectively.[25] A 5-carbonyl group in a des-A-steroid might be expected to be analogous to a 3-carbonyl group in a steroid but the bands at 1432 cm.$^{-1}$ in (A) and

Absorption maxima (cm.$^{-1}$).

(A)	1748	1720	1454 *		1432	1408	1375 *
(B)	1747	1725	1464	1449	1434	1410	1380 1374
Group	17-CO	5-CO	$-CH_2-$ (unperturbed)		6-CH_2–	16-CH_2–	CH_3–

* Broad maximum, probably two overlapping bands.

1434 cm.$^{-1}$ in (B) may reasonably be assigned to the 6-methylene groups since the two ranges of values are so close. At frequencies below 1350 cm.$^{-1}$ the absorption spectra of (A) and (B) are distinct and in view of this difference this work was discontinued.

Experimental

Optical rotations were measured with $CHCl_3$ as solvent unless otherwise stated. Alumina used was Type H from Messrs. Peter Spence and Co., except for one sample which was acid-washed and reactivated at 200—220° for 6 hr., after it had been found to be strongly alkaline.

Specimen Oxidation of Androst-4-ene-3 : 17-dione by Potassium Permanganate in Acetone.—Powdered potassium permanganate (2·0 g.) was added slowly to a stirred solution of androst-4-ene-3 : 17-dione (1·0 g.) in acetone (30 c.c.) at 0°, and the mixture was stirred at room temperature until the supernatant solution was colourless (1—2 hr.). The precipitated manganese oxides were collected, air-dried, and then stirred with ether (100 c.c.) and N-acetic acid (50 c.c.) while 30% hydrogen peroxide was added dropwise until no solid remained. The ethereal layer was dried and evaporated and the residue was heated for 15 min. at 100°, cooled, and treated with ethereal diazomethane (from *N*-nitrosomethylurea, 1·0 g.). The resulting solution was concentrated to 5 c.c., then kept at −10° overnight, and the product (0·22 g.), m. p. 235—239°, was collected and washed with methanol. *5-Methoxycarbonyl-4-oxa-androstane-3 : 17-dione* separated from methanol in plates, m. p. 239—240°, $[\alpha]_D^{18}$ +92°, $\nu_{max.}$ 1742 and 1733 cm.$^{-1}$ (Found: C, 69·2; H, 8·3. $C_{20}H_{28}O_5$ requires C, 68·9; H, 8·1%). If the crude product was not esterified it partly crystallised under ether at −20°, and after three crystallisations from aqueous

[24] Turner, *J. Amer. Chem. Soc.*, 1954, **76**, 1390.
[25] Jones and Cole, *ibid.*, 1952, **74**, 5648.

XUM

acetone (1 : 1) the *lactone acid* (X) was obtained in needles (0·04 g.), m. p. 257—262° (Found: C, 68·2; H, 7·7. $C_{19}H_{26}O_5$ requires C, 68·2; H, 7·8%). This acid with diazomethane gave the methyl ester, m. p. and mixed m. p. 238—239° (after crystallisation from methanol). The ester (0·22 g.), 0·25N-barium hydroxide (10 c.c.), and methanol (10 c.c.) were boiled for 3 days. The precipitate was collected, washed with methanol, suspended in water (4 c.c.), and treated with 2N-nitric acid (1·5 c.c.). The solid dissolved quickly and the resulting solution deposited the *hydroxy-dibasic acid* (IX) in needles (0·15 g.), m. p. 196—198° [with effervescence and formation of the lactone acid (X)] (Found: C, 64·7; H, 8·1. $C_{19}H_{28}O_6$ requires C, 64·8; H, 8·0%). Diazomethane converted this acid into a *dimethyl ester* which separated from ether–light petroleum (1 : 1) in needles, m. p. 152—153° (Found: C, 66·3; H, 8·5. $C_{21}H_{32}O_6$ requires C, 66·3; H, 8·5%). A solution of the dimethyl ester in methanol containing 2N-hydrochloric acid (1 drop) was heated at 50° for 2 hr. and cooled to room temperature, and the lactone ester separated in plates, m. p. and mixed m. p. 238—239°.

The residues from the preparation of the lactone ester were adsorbed on alumina (acid-washed; 30 g.). The column was washed with benzene [which eluted a substance crystallising from light petroleum in plates (*ca.* 2 mg.), m. p. 118—119°, not investigated further], and fractionally eluted with benzene–ether (9 : 1, 10 × 200 c.c.). Fractions 6 and 7 (*ca.* 0·1 g. each) partly crystallised during 2—3 weeks, and after trituration with ether (which was not discarded, see below) a *substance* (0·03 g.) was obtained which separated from acetone in needles, m. p. 209—212°, $\nu_{max.}$ 1744 and 1732 cm.$^{-1}$ (Found: C, 69·1; H, 7·9. $C_{20}H_{28}O_5$ requires C, 68·9; H, 8·1%). This substance is probably the $C_{(8)}$-epimer of the lactone ester rather than the methyl ester of the trioxo-acid (XI).

The ether washings from fractions 6 and 7 were evaporated, the residue in aqueous-methanolic (1 : 1) N-sodium hydroxide was boiled for 2 hr., and the resulting solution was neutralised with 2N-acetic acid, treated with semicarbazide hydrochloride, and left overnight at room temperature. The precipitate was washed with hot methanol, leaving the *bissemicarbazone* of the acid (V) as needles (0·1 g.), m. p. 270—280° (decomp.), identical (infrared spectra) with an authentic specimen (see below).

4ξ : 5ξ-*Dihydroxyandrostane*-3 : 17-*dione* (VII).—Androst-4-ene-3 : 17-dione (1·00 g.) and osmium tetroxide (0·05 g.) in ether (100 c.c.) were shaken for 5 min. with 30% hydrogen peroxide (2 c.c.) and then left for 36 hr. in the dark at room temperature. The ether was evaporated under reduced pressure, the residue was treated with water (5 c.c.), and acetone was added until the supernatant solution was clear. The solid was collected and crystallised from aqueous ethanol (1 : 2), to give the *diol* (VII) (0·18 g.), m. p. 210—216° (decomp.), which separated from ethanol in plates, m. p. 216—217·5° (decomp., rapid heating) or laths, m. p. 218—220° (decomp., rapid heating), $[\alpha]_D^{17\cdot5}$ +86° (Found: C, 71·1; H, 9·0. $C_{19}H_{28}O_4$ requires C, 71·2; H, 9·0%). The diol and acetic anhydride in pyridine at room temperature gave a *monoacetate*, needles (from ethanol), m. p. 236—237·5° (Found: C, 70·0; H, 8·5. $C_{21}H_{30}O_5$ requires C, 69·6; H, 8·3%). The yield of the diol was not improved by longer reaction times (after about three weeks colloidal osmium was formed), or by using more osmium tetroxide, or benzene or acetone as solvent. In acetone the reaction was very slow.

10-2′-*Carboxyethyldes*-A-*androstane*-5 : 17-*dione* (V).—(*a*) The diol (VII) (0·10 g.) in acetic acid (1 c.c.) was added to water (5 c.c.) and the resulting suspension was shaken for 5 min. with lead tetra-acetate (0·45 g.), then left at room temperature for 1 hr. 2N-Sulphuric acid was added slowly until no more lead sulphate was precipitated and the filtered solution was evaporated to dryness. The residue was extracted with ether and the extract was concentrated to a syrup. When the syrup was diluted with benzene and then with sufficient light petroleum to give an opalescent solution at 30—40°, the *acid* (V), with half a molecule of benzene of crystallisation, separated in large prisms (0·085 g.), m. p. 70—75° (unchanged after recrystallisation). The acid was purified by dissolving it in ice-cold N-sodium hydrogen carbonate, extracting the turbid solution with ether until clear, and then recovering and crystallising the acid (m. p. 73—75°) (Found: C, 73·4; H, 8·3. $C_{19}H_{28}O_4,\frac{1}{2}C_6H_6$ requires C, 73·0; H, 8·4%). When the solvated acid was dried at 100°/15 mm. for 1 hr. and left under light petroleum it resolidified after 2 months and then separated from dry ether as needles, m. p. 107—109° (Found: C, 70·3; H, 8·2. $C_{19}H_{28}O_4$ requires C, 70·6; H, 8·4%). The *bissemicarbazone* (prepared in pyridine) crystallised from aqueous pyridine in needles, m. p. 270—280° (decomp.) (Found: C, 56·9; H, 7·5. $C_{29}H_{32}O_4N_6$ requires C, 57·1; H, 7·7%).

(*b*) Finely powdered potassium permanganate (24·0 g.) was added during 1½ hr. to a stirred

solution of androst-4-ene-3 : 17-dione (20·0 g., m. p. 169—170·5°) in acetone (600 c.c.) at −6° to −8°, and the mixture was then stirred for 3 hr. at 0° and at room temperature for 1 hr. The manganese oxides were collected, air-dried, and dissolved in 50% acetic acid (100 c.c.) at 30°. The resulting dark brown solution was diluted with water (150 c.c.) and stirred at 30—35° until effervescence ceased (2—3 hr.), by which time the manganese oxides had reprecipitated. Hydrogen peroxide (30%; 12—14 c.c.) was added during ½ hr. (an excess was avoided), until the manganese oxides had redissolved, whereupon powdered potassium permanganate (16 g.) was added and the mixture was stirred at 30—35° until effervescence ceased. The manganese oxides were again brought into solution by the addition of hydrogen peroxide (30%; 40—45 c.c.), and the resulting solution was evaporated at 100°/15 mm. The semisolid residue was dissolved in hot 2N-acetic acid (150 c.c.), and the cold solution was extracted with chloroform (10 × 100 c.c.). The chloroform was evaporated, leaving crude acid (V), which was either crystallised (up to 7·0 g., m. p. 60—73°) from benzene–light petroleum or used directly in the next preparation.

10-2′-*Ethoxycarbonylethyldes*-A-*androstane*-3 : 17-*dione* (*ethyl ester of the acid* V).—The acid (V) (the crude product from the previous preparation; *ca.* 22 g.) in ethanolic 1% sulphuric acid (100 c.c.) was boiled for 2 hr., and the solution was concentrated to 40 c.c. and poured with shaking into N-sodium hydrogen carbonate (200 c.c.). An oil separated which soon solidified and was crystallised from methanol, to give the *ethyl ester* of the acid (V) (11—12 g., 47—51%; m. p. 104—107°), which separated from methanol after three more crystallisations in prisms, m. p. 107·5—109°, $[\alpha]_D^{17\cdot5}$ +91° (Found: C, 71·7; H, 8·9. $C_{20}H_{30}O_4$ requires C, 71·8; H, 9·0%). This ester was also obtained from the purified acid (V) by esterification with 1% ethanolic sulphuric acid and by diazoethane in ether.

4-*Oxa*-*androst*-5-*ene*-3 : 17-*dione* (XII).—The ethyl ester of the acid (V) (3·0 g.) and sodium hydroxide (0·45 g.) in aqueous methanol (1 : 1; 10 c.c.) were boiled for 2 hr. and evaporated to dryness at 100°/15 mm. Acetic anhydride (5 c.c.) was added to the residue and the mixture was boiled for 2 hr. and again evaporated to dryness. Dry toluene (5 c.c.) was added to the residue and evaporated, and this treatment was repeated until the residue no longer smelt of acetic anhydride (three evaporations usually sufficed). The product in dry benzene was filtered through neutral alumina (4 g.), the benzene was evaporated, and the residual oil crystallised when diluted with dry ether while still warm, giving 4-*oxa*-*androst*-5-*ene*-3 : 17-*dione* (2 crops; 2·4 g.), m. p. 136—143°, which separated from methanol, containing pyridine (1 drop in 5 c.c.), in prisms, m. p. 144—145°, $[\alpha]_D^{18}$ −71° (Found: C, 75·2; H, 8·4. $C_{18}H_{24}O_3$ requires C, 75·0; H, 8·4%).

17-*Acetoxy*-4-*oxa*-*androst*-5 : 16-*dien*-3-*one* (XIII).—The enol lactone (XII) (5·00 g.), toluene-*p*-sulphonic acid (0·30 g.), and *iso*propenyl acetate (25 c.c.) were boiled so that approximately 10 c.c. evaporated during 8 hr. The residue was diluted with benzene, filtered through alumina (15 g.; the acid being thereby neutralised), and evaporated. The residual oil crystallised under ether–methanol, to give the *enol acetate* (XIII) (5·2—5·4 g.), m. p. 146—150°, which separated from benzene–light petroleum in blades, m. p. 152—154° (Found: C, 72·3; H, 7·8. $C_{20}H_{26}O_4$ requires C, 72·7; H, 8·1%). A short time after purification this compound smelt of acetic acid.

Androst-4-*ene*-3 : 17-*dione* (III).—Ethereal methylmagnesium iodide (0·21M; 22 c.c., *ca.* 3·1 mol.) was added in small drops during 30 min. to a stirred solution of the enol acetate (XXVI) (0·495 g.) in benzene (20 c.c.) and ether (30 c.c.) under dry nitrogen at −15°, the solvents having been freshly distilled from sodium hydride directly into the reaction flask. The mixture was stirred while it came slowly to room temperature during 2 hr., then washed with 2N-sulphuric acid and with water, and the solvents were evaporated. The oily residue was left for 12 hr. with sodium hydroxide (1·0 g.) in water (2 c.c.) and methanol (20 c.c.); the resulting solution was diluted with water and extracted with ether. Evaporation of the ether gave crude androst-4-ene-3 : 17-dione (0·24 g.), m. p. 164—167°. After purification by chromatography on alumina androst-4-ene-3 : 17-dione separated from methanol in prisms, m. p. and mixed m. p. 171—172·5°, $[\alpha]_D^{21}$ +182° (Found: C, 79·5; H, 9·1. Calc. for $C_{19}H_{26}O_2$: C, 79·7; H, 9·1%). The infrared spectra and *X*-ray powder photographs of the authentic and the partially synthetic specimen were identical.

Synthetic androst-4-ene-3 : 17-dione (40 mg.), toluene-*p*-sulphonic acid (50 mg.), and *iso*propenyl acetate (5 c.c.) were boiled for 12 hr. The solution was diluted with dry ether, neutralised by filtration through alumina (2 g.), and evaporated. The residual oil was diluted

with boiling methanol (2 c.c.). **3 : 17-*Diacetoxyandrost*-3 : 5 : 16-*triene*** crystallised in needles, m. p. 137—138°, undepressed by an authentic specimen similarly prepared (Found: C, 74·2; H, 8·1. $C_{23}H_{30}O_4$ requires C, 74·6; H, 8·1%).

17-*Imino*-4-*aza*-*androst*-5-*en*-3-*one* (?) (XVII).—The ethyl ester of the acid (V) (2·0 g.) in ethanol (20 c.c.) was saturated with ammonia at 0° and the mixture was set aside at room temperature for 2 days. The imine (?) (XVII) was washed with ethanol and formed prisms, decomp. *ca.* 330° before and after crystallisation from ethanol (Found: C, 75·4; H, 8·6; N, 8·6. Calc. for $C_{18}H_{25}O_2N$: C, 75·3; H, 8·8; N, 4·8. Calc. for $C_{18}H_{26}ON_2$: C, 75·5; H, 9·1; N, 9·5%).

17-*Ethylenedioxy*-4-*aza*-*androst*-5-*en*-3-*one* (?) (XIX).—The imine (XVII) (0·30 g.), ethylene glycol (freshly distilled; 1·0 c.c.), and toluene-*p*-sulphonic acid (0·2 g.) were stirred for 2 hr. with slowly distilling benzene (volume maintained at *ca.* 20 c.c. while 200 c.c. distilled). The cooled residue was washed with N-sodium hydrogen carbonate and concentrated to 5 c.c. and cooled. The *ethylene ketal* (XIX) was collected and crystallised from benzene in plates (0·25 g.), m. p. 270—272° (Found: C, 72·4, 72·3; H, 9·0, 8·9; N, 4·3, 4·3. $C_{20}H_{29}O_3N$ requires C, 72·5; H, 8·8; N, 4·2%).

Reaction between the Ethyl Ester of the Acid (V) *and Ethyl Orthoformate.*—The ethyl ester of the acid (V) (0·50 g.), toluene-*p*-sulphonic acid (0·05 g.), ethyl orthoformate (1 c.c.), and ethanol (3 c.c.) were left at 30° for 12 hr. The resulting solution was shaken with benzene and N-sodium hydrogen carbonate, and the benzene layer was washed several times with water, dried, diluted with light petroleum, and filtered through neutral alumina (20 g.). The column was eluted with benzene which was evaporated and the residual oil crystallised under methanol, giving the *ketal* (?) (XXIII) in plates, m. p. 97—99°, $[\alpha]_D^{19}$ +49° (in EtOH) (Found: C, 72·9, 72·8; H, 9·6, 9·4. $C_{22}H_{34}O_4$ requires C, 72·9; H, 9·4%).

5 : 17-*Bisethylenedioxy*-10-(2-*ethoxycarbonylethyl*)-*des*-A-*androstane* (XXI).—The ethyl ester of the acid (V) (3·00 g.), ethylene glycol (5 c.c.), and toluene-*p*-sulphonic acid (0·10 g.) were stirred for 6 hr. with slowly distilling benzene (volume maintained at *ca.* 50 c.c. while 1 l. distilled). The cooled solution was washed with N-sodium hydrogen carbonate and evaporated, leaving an oil which crystallised under methanol to give the *ketal* (XXI) (3·00 g.). This separated from methanol in needles, m. p. 104—105·5°, $[\alpha]_D^{18}$ 0° (Found: C, 68·1; H, 9·2. $C_{24}H_{38}O_6$ requires C, 68·2; H, 9·1%).

5 : 17-*Bis*(*oxyethylenethio*)-10-(2-*ethoxycarbonylethyl*)-*des*-A-*androstane* (XXII).—Finely powdered 1 : 1 zinc chloride–sodium sulphate (5·0 g.) was added to the ethyl ester of the acid (V) (1·0 g.) and 2-mercaptoethanol (2 c.c.) in dry dioxan (5 c.c.). The semi-solid mass was left overnight, diluted with chloroform, and washed successively with water, 2N-sodium hydroxide (50 c.c.), and water. The chloroform was evaporated and the remaining syrup, when diluted with methanol, crystallised, giving the *ketal* (XXII) (0·88 g.), m. p. 100—110°, which, after purification by chromatography, separated from ethanol in needles, m. p. 113—115°, $[\alpha]_D^{18}$ 0° (Found: C, 63·2; H, 8·4. $C_{24}H_{38}O_4S_2$ requires C, 63·4; H, 8·4%).

17ξ-*Hydroxy*-4-*oxa*-*androstan*-3-*one* (XXIV, probably a mixture of isomers epimeric at positions 5 and 17).—The ethyl ester of the acid (V) (1·0 g.) and potassium hydroxide (0·4 g.) in methanol (10 c.c.) were boiled for 2 hr., cooled, and treated with potassium borohydride (0·2 g.) in water (1 c.c.). After being kept overnight at room temperature the solution was concentrated until crystallisation began, diluted with water (10 c.c.), and acidified with 12N-hydrochloric acid. The product was isolated with chloroform and crystallised from ether at 0°, to give the *hydroxy-lactone* (XXIV) (0·62 g.) as prisms, m. p. 143—168°, and needles, m. p. 118—159°, which were not separated (Found: C, 73·9; H, 9·8. $C_{18}H_{28}O_3$ requires C, 73·9; H, 9·6%).

5ξ : 17ξ-*Dihydroxy*-4 : 5-seco*androstan*-3-*one* (XXV, probably one isomer in the semiketal form XXVb).—The hydroxy-lactone (XXIV) (0·59 g.) and phenyl acetate (freshly distilled; 0·25 c.c.) were added to potassium (1·1 g.) dissolved in *tert.*-butyl alcohol (25 c.c.). Phenyl acetate (4·5 c.c., in 18 equal portions) was added at half-hourly intervals to the boiling solution, and boiling was then continued overnight. After water (10 c.c.) had been added, the butyl alcohol was slowly evaporated under reduced pressure and the precipitate was collected, boiled for 1 hr. with 2N-potassium hydroxide (10 c.c.), washed with water, and dried *in vacuo*. The solvated *ketone* (XXV) separated from methanol in prisms (0·18 g.), m. p. 171—172°, which were dried at room temperature (Found: C, 70·7; H, 10·3. $C_{19}H_{32}O_3,CH_4O$ requires C, 70·5; H, 10·7%). The methanol of crystallisation was readily removed in part at 100°/15 mm., but some remained even after 2 hr. at 140°/15 mm. and the substance became gummy when heated

XUM

longer (Found, after drying at 140°/15 mm.: C, 73·5; H, 10·3. Calc. for $C_{19}H_{32}O_3$: C, 74·2; H, 10·4%). This compound did not show an absorption band in the region 1650—1800 cm.$^{-1}$ and was assumed to exist in a lactol form.

10-(3-*Oxo*-3-*phenylpropyl*)-*des*-A-*androstane*-5 : 17-*dione* (XXVI).—Ethereal phenylmagnesium bromide (0·33M; 60 c.c.) was added in small drops during ½ hr. to a stirred solution of the enol lactone (XIII) (1·98 g.) in benzene (30 c.c.) and ether (50 c.c.) at −15° under dry nitrogen. The mixture was stirred for 1 hr. at −10°, washed with 2N-sulphuric acid (20 c.c.) and water, and evaporated. The residual oil crystallised under ether–methanol, to give the *phenyl ketone* (XXVI) (0·75 g.), m. p. 135—140° (a further 0·25 g., making a total yield of 45%, was isolated from the mother-liquors by chromatography), which separated from methanol in plates, m. p. 141—143°, $[\alpha]_D^{21}$ +110° (Found: C, 78·4; H, 8·3. $C_{24}H_{30}O_3$ requires C, 78·7; H, 8·2%).

Des-A-*androstane*-5 : 17-*dione* (I).—(*a*) The phenyl ketone (XXVI) (0·25 g.) was heated at 280—300°/15 mm. and then distilled at *ca.* 350°/10 mm. Volatile compounds were removed from the yellow distillate by steam-distillation and the dried residue was adsorbed on alumina. Elution with benzene–light petroleum (1 : 1) gave the *ketone* (I) which separated from light petroleum in prisms (5 mg.), m. p. 115—120°, undepressed by the specimen prepared as below.

(*b*) Pyrolysis of the barium salt of the acid (V) (prepared from the ethyl ester and barium hydroxide) at 320—340°/0·01 mm. in batches (1 g. or less) gave the *ketone* (I) which, after purification by chromatography, separated from light petroleum in prisms (10—20%), m. p. 119·5—120·5°, $[\alpha]_D^{21}$ +89° (Found: C, 76·7; H, 9·5. $C_{15}H_{22}O_2$ requires C, 76·9; H, 9·5%). This ketone was also obtained in very low yields (<1%) by pyrolysis of the ethyl ester of the acid (V) and by the action of potassium hydroxide in ethylene glycol on the phenyl ketone (XXVII) at 200°.

The ketone (I), in carbon tetrachloride, had absorption bands with $\nu_{max.}$ 1748, 1720, 1454, 1442, 1432, 1408, 1375, 1357, 1350, 1312, 1279, 1156, 1121, 1094, 1070, 1047, 955, 919, and 902 cm.$^{-1}$. After crystallisation from methanol Martin and Robinson's diketone, m. p. 130—131°, in carbon tetrachloride, had absorption bands at 1747, 1725, 1464, 1449, 1434, 1410, 1380, 1374, 1352, 1305, 1278, 1231, 1184, 1155, 1140, 1086, 1041, 1034, 942, and 933 cm.$^{-1}$.

The author thanks Sir Robert Robinson for suggesting and supervising this work and for his constant encouragement, and the Department of Scientific and Industrial Research and the Rockefeller Foundation for Maintenance grants. Optical measurements were made by Mr. F. Hastings.

THE DYSON PERRINS LABORATORY, OXFORD.
[Present Address: DEPARTMENT OF ORGANIC CHEMISTRY, THE UNIVERSITY OF LIVERPOOL.]

[*Received, March 21st,* 1957.]

---

467. *The Stereochemistry of Some* 1 : 5-*Diaza*cyclo*octane Derivatives.**

By R. KOLIŃSKI, (MISS) H. PIOTROWSKA, and T. URBAŃSKI.

The dipole moments of *cis*- and *trans*-3 : 7-diethyl-3 : 7-dinitro-1 : 5-diaza*cyclo*octane indicate that the ring is in the " crown " form. 3 : 7-Dialkyl-3 : 7-dinitro-1 : 5-diaza*cyclo*octanes form only monohydrochlorides and mononitroso-derivatives, which is considered to be due to internal hydrogen bonding: this is confirmed by infrared absorption spectra.

3 : 7 : 10-Triethyl-3 : 7 : 10-trinitro-1 : 5-diaza*bicyclo*[3 : 3 : 3]undecane is composed of two fused 1 : 5-diaza*cyclo*octane rings, which are held to a " double-chair " form on the basis of the dipole moment.

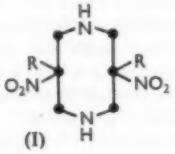
THE preparation of 3 : 7-dialkyl-3 : 7-dinitro-1 : 5-diaza*cyclo*octanes from primary nitroparaffins, formaldehyde, and ammonia has been described,[1] nitroethane, 1-nitropropane, and 1-nitrobutane yielding the compounds (I; R = Me, Et, and Pr^n respectively). We now show that the diethyl compound has the *trans*-configuration.

* Communicated at the 16th Congress of Pure and Applied Chemistry, Paris, 1957.

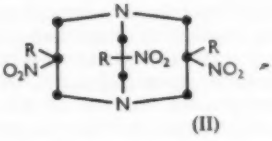
[1] Urbański and Lipska, *Roczniki Chem.*, 1952, **26**, 182; Urbański and Piotrowska, *ibid.*, 1955, **29**, 379; Jones, Koliński, Piotrowska, and Urbański, *ibid.*, 1957, **31**, 101.

XUM

1-Nitropropane also furnished the *cis*-isomer (I; R = Et), and a compound with two fused 1 : 5-diaza*cyclo*octane rings, namely, (II; R = Et).[2] On careful hydrolysis the latter gave a mixture of the *cis*- and the *trans*-isomer (I; R = Et). The same mixture was obtained when 2-hydroxymethyl-2-nitrobutan-1-ol was warmed with an excess (5 mol.) of



(I)



(II)

ammonia. The isomers were separated by virtue of the greater solubility of the *cis*-hydrochloride (it is interesting that free *cis*-amine was the *less* soluble isomer).

Although chemical proof of the structures (I) and (II) was given earlier,[1,2] we considered it advisable to check the structures by determining the molecular refractions of the compounds: these proved to be in agreement with calculated figures see Table.

	M_R		NH frequencies (cm.$^{-1}$)				NO_2 frequencies (cm.$^{-1}$) *	
			Stretching			Deformn.		
Compound	Expt.	Calc.	Free	Free (?)	Bonded		Free	Bonded
I; R = Me	56·20	56·30	3448	3295	3228	1613w	1361s	1325
cis-I; R = Et	65·83	65·53	3475	3320	3190	1681w	1361	—
trans-I; R = Et ...	65·90	65·53	3475	3320	3228	1653w	1351	1333sh
I; R = Pr^n	74·95	74·76	3475	3320	3220	1653	1361	1333sh
II; R = Et	92·50	92·16	—	—	—	—	—	—

(w = weak, s = strong, sh = shoulder)

* For the region of asymmetric NO_2 vibrations (6·5 μ) *cyclo*hexane solutions were used. The thin layer (1 mm.) required a relatively high concentration (0·025 mole l.$^{-1}$). Two frequencies were found 1563—1587 (free NO_2) and 1538 cm.$^{-1}$ (bonded NO_2). As the dilution was probably insufficient to break intermolecular hydrogen bonds, these figures have not been considered in our discussion.

The diaza*cyclo*octanes (I) form only monohydrochlorides and mononitroso-derivatives, believed[3] to be due to internal hydrogen bonding between the two secondary nitrogen atoms (>NH · · · NH<) or between one of the amino- and one of the nitro-groups. Infra-red absorption spectra have now brought evidence of both free and bonded NH and NO_2 groups. The Table shows the maxima for CCl_4 solutions and their assignments. Three NH bands have been found in the region of higher frequencies (*ca.* 3475, 3320, and 3200 cm.$^{-1}$). Since internal hydrogen-bonding produces a small fall of frequency (usually less than 100 cm.$^{-1}$),[4] we assign the frequencies 3475 and 3320 cm.$^{-1}$ to free and the frequency 3200 cm.$^{-1}$ to bonded NH groups. For the nitro-groups two frequencies of symmetric vibrations have been noticed: one corresponding to the free nitro-group, the other, lower by 18—36 cm.$^{-1}$, to the bonded nitro-group, in accordance with earlier work.[3] Work on the hydrochlorides and nitroso-derivatives is in progress.

In a study of the stereochemistry various ring forms were by means of molecular models found to be impossible. Finally three ring forms needed consideration: the crown form (*A*) (Fig. 1), the double-chair form (*B*), and the skew form (*C*).

Dipole moments were calculated and measured for derivatives of 1-nitropropane, *i.e.*, the *cis*- and the *trans*-isomer (I; R = Et) and compound (II; R = Et), which were conveniently soluble in benzene. Group moments NH 1·3 D and NO_2 3·5 D, and the

[2] Jones, Koliński, Piotrowska, and Urbański, *Bull. Acad. polon. Sci.*, Cl. III, 1956, **4**, 521; *Roczniki Chem.*, 1957, **31**, 101.

[3] Urbański, *Bull. Acad. polon. Sci.*, Cl. III, 1953, **1**, 239; 1954, **2**, 393; 1956, **4**, 87, 381; 1957, **5**, 533; Urbański and Ciecierska, *Roczniki Chem.*, 1955, **29**, 11; Urbański, *ibid.*, p. 375; 1957, **31**, 37.

[4] Bellamy, " The Infra-red Spectra of Complex Molecules," Methuen & Co., London, 1956, p. 215

CNC angle 110° were assumed in calculations. The experimental value for *trans*-isomer was found to be 5·4 D, which fitted to form (*A*) with two possible conformations of two nitro-groups, namely, axial and equatorial (*i.e.*, *trans*) (μ = 5·4 D) (Fig. 2), and both axial (*i.e.*, *cis*) (μ = 6·0 D) (Fig. 3, where all possible hydrogen bonds are shown on one diagram).

By analogy with *cyclo*hexane derivatives a form with equatorial conformation should be considered more probable, so preference is given to the conformation of Fig. 2.

FIG. 1.

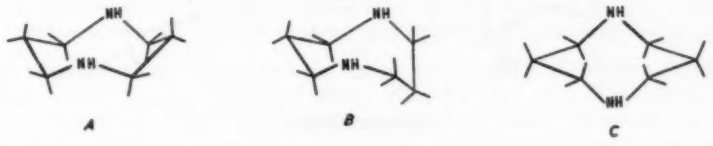


FIG. 2.

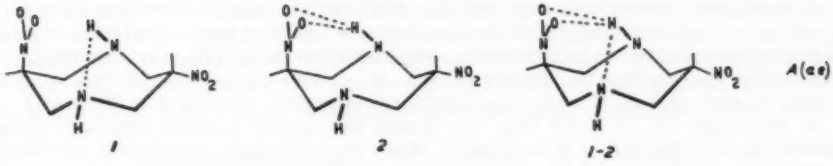


FIG. 3.

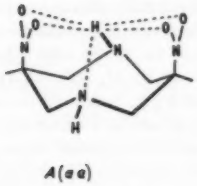
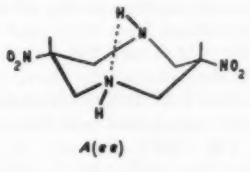


FIG. 4.



In either form a NO_2–HN hydrogen bond would be possible, the distance between H and O being *ca.* 2·5 Å. Only one bond of the type $>NH \cdots NH<$ is possible in form (*A*) (bond length *ca.* 2·0 Å).

If both nitro-groups were equatorial (*i.e.*, *cis*) in form (*A*) (Fig. 4) the calculated value of μ was 4·3 D. This is in agreement with the experimental value (4·6 D) for the *cis*-isomer (I; R = Et).

It is evident that the conformation of Fig. 4 could be obtained from that of Fig. 3 by a simple ring conversion. As equatorial conformations are more likely, the latter is more stable and therefore more probable.

Consequently, we accept conformation ae of Fig. 2 for the *trans*- and conformation ee of Fig. 4 for the *cis*-isomer (I; R = Et).

The two other forms (*B*) and (*C*) of Fig. 1 should be rejected, because the calculated values of the dipole moment were lower than the experimental figures. Thus, for form (*B*) the values for different conformations of nitro- and ethyl groups were 3·0, 3·6, and 3·5 D. For form (*C*) values were calculated to be 1·9, 3·2, 0, and 3·5 D. It has been established by means of models that the bicyclic compound (II; R = Et) can exist in two forms only: both possess B rings and conformation of the nitro-group is either symmetric (Fig. 5) or asymmetric (Fig. 6). Their calculated dipole moments are 0 and 5·5 D respectively. The experimental value was 5·7 D. Thus, the asymmetric structure (Fig. 6) should be accepted.

It should be pointed out that the 1 : 5-diaza*cyclo*octane ring occurs in sparteine and a number of similar alkaloids.[5] Further analogy with sparteine exists in substitution of these rings in the positions 3 and 7.

FIG. 5.

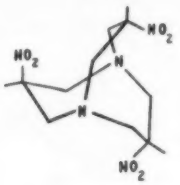
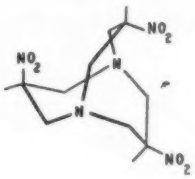


FIG. 6.



EXPERIMENTAL

3 : 7-*Diethyl*-3 : 7-*dinitro*-1 : 5-*diaza*cyclo*octane Hydrochlorides*.—(*a*) 2-Hydroxymethyl-2-nitrobutan-1-ol (15 g., 0·1 mol.) was kept in 25% aqueous ammonia (34 ml., 0·5 mol.) for 1 hr. on a steam-bath. Resin separated and was dissolved in alcoholic hydrogen chloride. A mixture of *cis*- and *trans*-hydrochlorides separated at 0° during 3 days. Fractional crystallisation from alcohol gave the less soluble *trans*-hydrochloride, m. p. 172—173° (decomp.). The more soluble fraction was the cis-*hydrochloride*, m. p. 169—171° (decomp.) (0·07 g., 0·5%) (Found: C, 40·5; H, 7·2; N, 19·1. $C_{10}H_{20}O_4N_4$,HCl requires C, 40·4; H, 7·1; N, 18·8%).

(*b*) The amine (II; R = Et) (2 g.) was heated on a steam-bath with ethanolic hydrogen chloride (15 ml.), then left at 0° overnight. Mixed hydrochlorides (1·3 g.) were precipitated; fractionation as in the method (*a*) gave the *cis*-hydrochloride, m. p. 169—171° (decomp.) (0·15 g., 11%).

cis-3 : 7-*Diethyl*-3 : 7-*dinitro*-1 : 5-*diaza*cyclo*octane*.—The *cis*-base was prepared by neutralisation of an aqueous solution of the *cis*-hydrochloride with sodium hydroxide and extraction with ether; crystallised from ether and then alcohol, it had m. p. 94—95° [Found: C, 46·2; H, 7·7; N, 21·8%; *M* (Rast), 254. $C_{10}H_{20}O_4N_4$ requires C, 46·1; H, 7·7; N, 21·6%; *M*, 260].

cis-*N*-*Nitroso-derivative*.—The above *cis*-hydrochloride (0·2 g.), dissolved in small amount of water, was acidified with 10% hydrochloric acid, and 20% aqueous sodium nitrite was added. The solid *N-nitroso-compound* was extracted with ether and crystallised from ethanol (yield, 0·1 g.; m. p. 139—140°) (Found: N, 24·4. $C_{10}H_{19}O_5N_5$ requires N, 24·2%). With concentrated hydrochloric acid at 60° it yielded the hydrochloride of the *cis*-isomer (I; R = Et).

Dipole Moments.—These were measured by the heterodyne beat method, with benzene as a solvent. The results were extrapolated by the method of Le Fèvre and Vine.

Infrared Absorption Spectra.—The spectra were measured by means of Hilger single-beam spectrophotometer type H-668, for CCl_4 solutions (0·0025—0·005 mole $l.^{-1}$) in 5 cm. layers. The optics were of sodium chloride: for the range 2·5—3·5 μ optics of lithium fluoride were used.

Molecular Refractions.—These were determined from refractive indexes, measured in benzene, dioxan, or carbon tetrachloride. The results for various solvents were the same within experimental error.

We are much indebted to Professor D. Ginsburg of Haifa Technion for supplying us with atomic models (Catalin Products Ltd.). We thank also Professor W. Tomassi, Dr. H. Calus, and Miss H. Jankowska for measuring the dipole moments, Mr. T. Traczyk for calculating some of the dipole moments, and Dr. (Mrs.) J. Świętosławska, Miss B. Kontnik, and Miss T. Kraczkiewicz for measuring the infrared spectra.

INSTITUTE OF ORGANIC SYNTHESIS, POLISH ACADEMY OF SCIENCES,
WARSAW 10, POLAND.

[*Received, July* 16*th*, 1957.]

[5] Clemo, Morgan, and Raper, *J.*, 1936, 1025.

XUM

468. *Platinum*(0) *Compounds with Triarylphosphines and Analogous Ligands.*

By L. Malatesta and (Miss) C. Cariello.

Some new derivatives of platinum in a zero oxidation state with triarylphosphines and -arsines and triaryl phosphites are described. Some of these compounds are co-ordinatively saturated, *i.e.*, of the type $Pt^0(PAr_3)_4$; others are unsaturated, of the type $Pt^0(PAr_3)_3$.

The phosphine derivatives react with carbon monoxide giving mixed carbonyl phosphine derivatives of the type $Pt(CO)(PAr_3)_3$ and $Pt(CO)(PAr_3)_2$.

Since there is a close analogy between the complex compounds of palladium and platinum in the same oxidation state it seemed likely, after the discovery of stable palladium(0) complexes,[1] that similar complexes of platinum(0) should exist. However, we have been unable to obtain $Pt(CNR)_2$ analogous to $Pd(CNR)_2$, the first palladium(0) compound to be reported, nor any other individual compound from the reduction of either isomer of $Pt(CNR)_2X_2$ (X = Cl, Br, I).[2] Nevertheless, we have now obtained platinum(0) complexes with tervalent phosphorus as ligand atom.[3]

Triarylphosphine Derivatives of Platinum(0).—The dihalogenobis(triphenylphosphine)-platinum(II), in the presence of an excess of triphenylphosphine, can be reduced quantitatively to platinum(0) compounds with anhydrous hydrazine, which reacts as follows:

$$PtI_2(PPh_3)_2 + 2{\cdot}5H_2N{\cdot}NH_2 + 2PPh_3 = Pt(PPh_3)_4 + 0{\cdot}5N_2 + 2H_2N{\cdot}NH_3I$$

Tetrakis(triphenylphosphine)platinum(0) can also be obtained, as in the case of palladium, either from dihalogenobis(triphenylphosphine)platinum(II), triphenylphosphine and ethanolic potassium hydroxide, or from chloroplatinate(II), triphenylphosphine, and ethanolic potassium hydroxide.

The reducing agent could be either phosphine:

$$PtX_2(PPh_3)_2 + 3PPh_3 + 2KOH = Pt(PPh_3)_4 + O{:}PPh_3 + 2KX + H_2O$$

$$K_2PtCl_4 + 2KOH + 5PPh_3 = Pt(PPh_3)_4 + O{:}PPh_3 + 4KCl + H_2O$$

or the potassium ethoxide.

Tetrakis(triphenylphosphine)platinum(0) is yellow, crystalline, soluble in benzene and chloroform, almost insoluble in ethanol, and stable to air for many hours. Cryoscopy in benzene shows a dissociation which increases with time, possibly due to replacement of part of the phosphine by the solvent.

Platinum appears to form these zero-valent compounds even more readily than palladium, since, while the dihalogenobis(triphenylphosphine)palladium(II) reacts with hydrazine (without excess of ligand) giving metallic palladium, yet the dihalogenobis(triphenylphosphine)platinum(II) under the same conditions disproportionates forming unsaturated platinum(0) compounds:

$$4PtI_2(PPh_3)_2 + 3H_2N{\cdot}NH_2 = 2Pt(PPh_3)_3 + Pt_2I_4(NH_2{\cdot}NH_2)_2(PPh_3)_2 + N_2 + 4HI$$

Tris(triphenylphosphine)platinum(0) is yellow, crystalline, stable to air, and soluble in benzene in which it dissociates. The product written as $Pt_2I_4(NH_2{\cdot}NH_2)_2(PPh_3)_2$ will be discussed elsewhere.

When tri-*p*-chlorophenylphosphine instead of triphenylphosphine complexes are reduced only the trico-ordinate Pt^0 derivative $Pt[P(p\text{-}Cl{\cdot}C_6H_4)_3]_3$ is obtained, as happened with palladium.[1]

Triarylarsine Derivatives of Platinum(0).—Platinum(0) compounds with triarylarsines are analogous to the saturated ones with triarylphosphines. They could be obtained only

[1] Malatesta, *J.*, 1956, 3924; Malatesta and Angoletta, *J.*, 1957, 1186.
[2] Tschugaev and Teearu, *Ber.*, 1914, **47**, 568.
[3] Malatesta and Angoletta, *Atti Accad. naz. Lincei, Rend. Classe Sci. Fis. Mat.*, 1955, **19**, 43.

XUM

by reduction of the dihalogenobis(triarylarsine)platinum(II) with hydrazine and an excess of ligand. They are very similar to, but much less stable than, the phosphine compounds of the same series.

Triaryl Phosphite Derivatives of Platinum(0).—Reaction of dihalogenobis(triphenyl phosphite)platinum(II) with ethanolic hydrazine and excess of triphenyl phosphite gives tetrakis(triphenyl phosphite)platinum(0). This is a white crystalline product, stable to air, and very soluble in benzene and chloroform, in which it largely dissociates. Tri-*p*-chlorophenyl phosphite behaves analogously. The same reaction, without excess of the phosphite, gives, analogously to the phosphines, the trico-ordinated compound $Pt[P(OPh_3)]_3$ which is white, crystalline, stable to air, and dissociated in benzene.

The tetrakis(triphenyl phosphite) derivatives can also be obtained from the triphenylphosphineplatinum(0) derivatives and triphenyl phosphite by ligand exchange:

$$Pt(PPh_3)_4 + 4P(OPh)_3 = Pt[P(OPh)_3]_4 + 4PPh_3$$

On the other hand tris(tri-*p*-chlorophenylphosphine)platinum(0), even in the presence of a large excess of triphenyl phosphite, gives a tetraco-ordinated platinum(0) compound with three molecules of phosphite and a molecule of phosphine. With the triphenylphosphine complex, mixed products can be prepared only by reaction of the platinum–phosphine derivative with the stoicheiometric amount, *i.e.*, 3 moles, of the phosphite.

List of the Pt(0) *compounds prepared.*

Compound	Colour	M. p. or decomp. pt.
$Pt^0(PPh_3)_4$	Ivory-yellow	118°
$Pt^0(PPh_3)_3$	Yellow	125—130
$Pt^0[P(p\text{-}Cl\cdot C_6H_4)_3]_3$	Golden-yellow	186
$Pt^0(AsPh_3)_4$	Colourlesss	183
$Pt^0[As(p\text{-}Cl\cdot C_6H_4)_3]_4$	,,	178
$Pt^0[P(O\cdot Ph)_3]_4$	,,	145
$Pt^0[P(O\cdot Ph)_3]_3$	Ivory-yellow	120—124
$Pt^0[P(O\cdot C_6H_4\cdot Cl\text{-}p)_3]_4$	Colourless	163
$Pt^0(p\text{-}Cl\cdot C_6H_4)_3[P(O\cdot Ph)_3]_3$	,,	157
$Pt^0P(PPh_3)_3[P(O\cdot C_6H_4\cdot Cl\text{-}p)_3]_3$	,,	141
$Pt^0(CO)_3(PPh_3)_3$	,,	118 *
$Pt^0(CO)(PPh_3)_3$	Orange	130
$Pt^0(CO)_3[P(p\text{-}Cl\cdot C_6H_4)_3]_3$	Colourless	—
$Pt^0(CO)[P(p\text{-}Cl\cdot C_6H_4)_3]_3$	Orange	141

* Mixed with $2PPh_3$.

Carbonylphosphine Derivatives of Platinum(0).—The platinum(0) derivatives were treated with carbon monoxide under pressure in an attempt to prepare platinum(0) derivatives analogous to those of nickel, which had been obtained by action of phosphines and phosphites on nickel tetracarbonyl.[4] Carbon monoxide does not react with the phosphite compounds, and gives dicarbonyl derivatives with the phosphine compounds.

As the co-ordination number of platinum(0) is unlikely to exceed four, one must assume that the following reactions have taken place:

$$Pt(PPh_3)_4 + 2CO = Pt(CO)_2(PPh_3)_2 + 2PPh_3$$

$$Pt(PPh_3)_3 + 2CO = Pt(CO)_2(PPh_3)_2 + PPh_3$$

The phosphine displaced by the carbon monoxide cannot be removed from the reaction mixture because, if one tries to dissolve it in a solvent, it reacts with the product, substituting one of the two carbon monoxide molecules:

$$Pt(CO)_2(PPh_3)_2 + PPh_3 = Pt(CO)(PPh_3)_3 + CO$$

When the reaction product of tris-(*p*-chlorophenylphosphine)platinum(0) with carbon monoxide is dissolved in diethyl ether it gives the co-ordinatively unsaturated compound

[4] Malatesta and Sacco, *Ann. Chim.*, 1954, **44**, 134.

$Pt(CO)[(p\text{-}Cl\cdot C_6H_4)_3P]_2$. This may be formed either by the action of the solvent on a primary co-ordinatively saturated compound:

$$Pt(CO)_2[(p\text{-}Cl\cdot C_6H_4)_3P]_2 = Pt(CO)[(p\text{-}Cl\cdot C_6H_4)_3P]_2 + CO$$

or by reaction of a co-ordinatively unsaturated, primary compound with the displaced phosphine:

$$Pt(CO)_2(p\text{-}Cl\cdot C_6H_4)_3P + (p\text{-}Cl\cdot C_6H_4)_3P = Pt(CO)[(p\text{-}Cl\cdot C_6H_4)_3P]_2 + CO$$

The primary reaction mixtures of the dicarbonyl derivatives and phosphine are crystalline and light yellow. They slowly lose carbon monoxide and melt at the same temperature as the original phosphine derivatives. The monocarbonyl derivatives are orange-yellow; they can be recrystallized, and melt without decomposition.

Experimental

(A) *Intermediates.*—(I) *Di-iodobis(triphenylphosphine)platinum*(II), $PtI_2(PPh_3)_2$. A saturated xylene solution of triphenylphosphine (7·8 g., 3 mmoles) and platinous iodide (4·5 g., 1 mmole) were refluxed for about 6 hr. The warm solution was filtered and concentrated to half its original volume. On cooling, orange-yellow crystals soluble in benzene and chloroform, insoluble in hexane and ethanol, were obtained; m. p. 285° (Found: Pt, 20·0; P, 6·2; I, 26·3. $C_{36}H_{30}I_2P_2Pt$ requires Pt, 20·0; P, 6·1; I, 26·1%). This *complex* exists also in a high-temperature form, which can be obtained as brick-red crystals by rapidly cooling the xylene solution.

Analogously prepared were:

(II) *Di-bromobis(triphenylphosphine)platinum*(II), orange crystals, decomp. at 300°. The same product was obtained by treating the tetrakis(triphenylphosphine)platinum(0) compound with calculated amount of bromine: $Pt(PPh_3)_4 + Br_2 = PtBr_2(PPh_3)_2 + 2PPh_3$ (Found: Pt, 24·2; P, 7·5; Br, 19·7. $C_{36}H_{30}P_2Pt$ requires Pt, 24·7; P, 7·7; Br, 20·0%).

(III) *Di-chlorobis(triphenylphosphine)platinum*(II) [from K_2PtCl_4 (2·2 g., 1 mmole) and triphenylphosphine (3·9 g., 3 mmoles)], white crystals, which blacken above 300° without melting; soluble in chloroform and benzene, insoluble in ethanol and diethyl ether (Found: Pt, 24·1; P, 8·0; Cl, 8·9. $C_{36}H_{30}Cl_2P_2Pt$ requires Pt, 24·4; P, 7·8; Cl, 8·9%).

(IV) *Di-iodobis(tri-*p*-chlorophenylphosphine)platinum*(II), very similar to (I); orange crystals, m. p. 288° (Found: Pt, 16·6; P, 5·1; I, 22·0. $C_{36}H_{24}Cl_6I_2P_2Pt$ requires Pt, 16·5; P, 5·2; I, 21·5%).

(V) *Di-iodobis(tri-*p*-methoxyphenylphosphine)platinum*(II), pale yellow crystals, decomp. 250—255° (Found: Pt, 16·7; P, 5·2; I, 21·7. $C_{42}H_{42}O_6I_2P_2Pt$ requires Pt, 16·9; P, 5·4; I, 22·0%).

(VI) *Di-iodobis(tri-*p*-tolylphosphine)platinum*(II), pale yellow crystals, m. p. 263° (Found: Pt, 18·2; P, 5·7; I, 23·6. $C_{42}H_{42}I_2P_2Pt$ requires Pt, 18·5; P, 5·9; I, 23·9%).

(VII) *Di-iodobis(triphenylphosphine)platinum*(II). From Chatt's work [5] this *compound* must be considered dimeric with two iodo-bridges, *i.e.*, di-μ-iodobis[iodo(triphenylphosphine)-platinum(II)]. It was prepared by refluxing compound (I) and an excess of platinous iodide in xylene for several hours; it was then extracted with, and crystallized from, chloroform; dark-red crystals, decomp. >300° without melting (Found: Pt, 26·6; I, 35·2; P, 4·4. $C_{18}H_{18}I_2PPt$ requires Pt, 27·4; I, 35·7; P, 4·5%).

(VIII) *Di-iodobis(triphenyl phosphite)platinum*(II). This was prepared by refluxing for a few minutes platinous iodide (2·2 g., 1 mmole) and triphenyl phosphite (3·8 g., 2·5 mmoles) in xylene (about 20 ml.). The hot solution was then filtered, and 3 vols. of ethanol added. The *compound* crystallized as pale yellow tablets, insoluble in ethanol and hexane. On warming it turns red (perhaps giving the isomeric form) and melts at 201° (Found: Pt, 18·8; P, 5·8; I, 23·9%; *M*, cryoscopic in 2% benzene solution, 1020. $C_{36}H_{30}O_6I_2P_2Pt$ requires Pt, 18·3; P, 5·8; I, 23·7%; *M*, 1068).

(IX) *Di-iodobis(tri-*p*-chlorophenyl phosphite)platinum*(II), prepared as for the previous compound and having similar properties; m. p. 215—220° (Found: Pt, 15·5; P, 4·9. $C_{36}H_{24}O_6Cl_6I_2P_2Pt$ requires Pt, 15·3; P, 4·9%).

(X) *Di-iodobis(triphenylarsine)platinum*(II). This was prepared by refluxing platinous

[5] Chatt and Venanzi, *J.*, 1955, 2787.

iodide (2·2 g., 1 mmole) and triphenylarsine (4·5 g., 3 mmoles) in xylene for several hours. The hot solution was filtered and, on cooling, crystals of apricot-like colour were obtained. It is soluble in benzene, chloroform, and hot ethanol; m. p. 276° (Found: Pt, 18·1; As, 14·4; I, 23·4. $C_{36}H_{30}I_2As_2Pt$ requires Pt, 18·4; As, 14·2; I, 23·9%).

Similarly prepared were: (XI) *Dichlorobis(triphenylarsine)platinum*(II) [from K_2PtCl_4 (4·3 g., 1 mmole) and triphenylarsine (9·2 g., 2·5 mmoles)], pale-yellow crystals, m. p. 278°, soluble in benzene and chloroform, almost insoluble in alcohol and hexane (Found: Pt, 21·7; As, 17·2. $C_{36}H_{30}Cl_2As_2P$ requires Pt, 22·2; As, 17·1%). (XII) *Di-iodobis(tri-p-chlorophenylarsine)platinum*(II), pink crystals, m. p. 285° (Found: Pt, 15·6; Cl, 16·6; I, 20·1; As, 11·0. $C_{36}H_{24}Cl_6I_2As_2Pt$ requires Pt, 15·4; Cl, 16·8; I, 20·0; As, 11·8%). (XIII) *Dichlorobis(tri-p-chlorophenylarsine)platinum*(II), lemon-yellow crystals, m. p. 279° (Found: Pt, 19·6; As, 13·8. $C_{36}H_{24}Cl_8As_2Pt$ requires Pt, 19·0; As, 13·8%). (XIV) *Dichlorobis(tri-p-tolylarsine)platinum*(II), m. p. 289° (Found: Pt, 20·1; As, 16·4. $C_{42}H_{42}Cl_2As_2Pt$ requires Pt, 20·4; As, 16·0%). (XV) *Dichlorobis(tri-p-methoxyphenylarsine)platinum*(II), green-yellow crystals, m. p. 248° (Found: Pt, 18·1; As, 13·9; Cl, 6·5. $C_{42}H_{42}O_6Cl_2As_2Pt$ requires Pt, 18·4; As, 14·2; Cl, 6·7%).

(B) *Platinum*(0) *Compounds with Arylphosphines as Ligands.*—(XVI) *Tetrakis(triphenylphosphine)platinum*(0). (*a*) From K_2PtCl_4, PPh_3, and KOH: A saturated aqueous solution of K_2PtCl_4 (2·2 g., 1 mmole) was slowly added, with vigorous stirring, to a warm (50—60°) saturated ethanolic solution of triphenylphosphine (6·5 g., 5 mmoles) containing potassium hydroxide (0·6 g., 2·5 mmoles). Yellow crystals separated almost immediately. The solution was kept for a few minutes on the water-bath and then filtered. The precipitate was washed first with warm ethanol, then with cold water, and finally with ethanol, and dried in a vacuum.

(*b*) From $PtCl_2(PPh_3)_2$, $H_2N{\cdot}NH_2$, and excess of PPh_3: $PtCl_2(PPh_3)_2$ (4·0 g., 1 mmole) and triphenylphosphine (4 g., 3 mmoles) suspended in ethanol (20 ml.) were warmed to 70—80° and then treated slowly with 10 ml. of 10% ethanolic anhydrous hydrazine. The suspended platinum(II) derivative dissolved slowly with a brisk evolution of gas. After a few minutes the crystalline platinum(0) compound started to separate. It was filtered off, washed, and dried as described previously. The same product can be obtained from the bromo-derivative (II) and the iodo-derivative (I). It was recrystallized by addition of hexane to a cold saturated benzene solution (Found: Pt, 15·6; P, 9·9%; *M*, cryoscopic in 2·2% benzene solution, 400. $C_{72}H_{60}P_4Pt$ requires Pt, 15·7; P, 10·0%; *M*, 1178). Recrystallization from chloroform gave a compound which contained less phosphine and some solvent of crystallization (Found: Pt, 16·2; P, 9·8; Cl, 2·5%). *Tetrakis(triphenylphosphine)platinum*(0) is soluble in benzene and chloroform and almost insoluble in ethanol and hexane. It is stable in air for some hours, and completely stable in nitrogen. It reacts with bromine in chloroform solution, giving the dibromide (II).

(XVII) *Tris(triphenylphosphine)platinum*(0). By proceeding as for compound (XVI, *b*), from the iodide (III) but without free phosphine, a yellow crystalline *product* was obtained (Found: Pt, 19·9; P, 9·4%; *M*, cryoscopic in 2·5% benzene solution, 450. $C_{54}H_{45}P_3Pt$ requires Pt, 19·9; P, 9·5%; *M*, 981). On concentrating the filtrate under reduced pressure, white crystals separated, which decomposed on standing with separation of metallic platinum. These contained Pt : PPh_3 : N : I ~ 1 : 1 : 1 : 2 but were not further investigated.

(XVIII) *Tris(tri-p-chlorophosphine)platinum*(0). Prepared as for (XVI) and (XVII), but with tri-*p*-chlorophosphine, this *complex* formed golden-yellow leaflets, indefinitely stable in air, soluble in benzene and chloroform (Found: Pt, 15·4; P, 7·2; Cl, 24·8. $C_{54}H_{36}Cl_9P_3Pt$ requires Pt, 15·1; P, 7·2; Cl, 24·7%).

(C) *Platinum*(0) *Compounds with Arylarsines as Ligands.*—(XIX) *Tetrakis(triphenylarsine)platinum*(0). A 10% solution of anhydrous hydrazine in butanol (5 ml.) was slowly added to a suspension of compound (XI) (4·4 g., 1 mmole) and triphenylarsine (4·6 g., 3 mmoles). A brisk evolution of nitrogen took place and the suspended yellow crystals turned pearly white. (Prolonged heating is apt to cause formation of metallic platinum.) The crystals were washed with warm ethanol and dried under reduced pressure. The *complex* is soluble in benzene and chloroform with partial decomposition, insoluble in ethanol and hexane (Found: Pt, 13·6; As, 21·0. $C_{72}H_{60}As_4Pt$ requires Pt, 13·7; As, 21·1%).

(XX) *Tetrakis(tri-p-chlorophenylarsine)platinum*(0), prepared from (XIII) analogously to the previous compound, in ethanol, formed golden-yellow crystals (Found: Pt, 10·7; As, 16·5; Cl, 23·1. $C_{72}H_{48}Cl_{12}As_4Pt$ requires Pt, 10·7; As, 16·5; Cl, 23·4%).

(D) *Platinum*(0) *Compounds with Triaryl Phosphites as Ligands.*—(XXI) *Tetrakis(triphenyl*

XUM

phosphite)platinum(0). The compound (VIII) (5·4 g., 1 mmole) and triphenyl phosphite (3·9 g., 2·5 mmoles), suspended in ethanol (20 ml.), were treated slowly at 70—80° with a 10% ethanolic solution of anhydrous hydrazine, until the crystals wholly disappeared. After filtering and cooling, the *product* separated as white crystals, soluble in cold benzene and chloroform and in warm ethanol and stable to dry air (Found: Pt, 13·3; P, 8·65. $C_{72}H_{60}O_{12}P_4Pt$ requires Pt, 13·6; P, 8·65%).

(XXII) *Tris(triphenyl phosphite)platinum*(0), prepared as above but without addition of triphenyl phosphite, is very similar to compound (XXI) (Found: Pt, 17·1; P, 8·4. $C_{54}H_{45}P_3Pt$ requires Pt, 17·3; P, 8·3%).

(XXIII) *Tetrakis(tri*-p-*chlorophenyl phosphite)platinum*(0) was prepared as for compound (XXI), from $PtCl_2[P(O{\cdot}C_6H_4{\cdot}Cl\text{-}p)_3]_2$ (5·5 g., 1 mmole), $P(O{\cdot}C_6H_4{\cdot}Cl\text{-}p)_3$ (5·1 g., 2·5 mmoles), and hydrazine (Found: Pt, 10·6; P, 6·9; Cl, 22·6. $C_{72}H_{48}O_{12}Cl_{12}P_4Pt$ requires Pt, 10·6; P, 6·7; Cl, 23·0%).

(E) *Reactions between the Tris- and Tetrakis-(triarylphosphine)platinum*(0) *and the Triaryl Phosphites.*—Both tris- and tetrakis-(triphenylphosphine)platinum(0) reacted with a slight excess of triphenyl phosphite in warm ethanolic solution, yielding $Pt[P(OPh)_3]_4$ as pure crystals. The m. p. of the compound prepared by ligand exchange was 146°, mixed m. p. with (XXI) 145·5°.

Tetrakis(triphenylphosphine)platinum(0) (3·1 g., 1 mmole) in ethanolic suspension (20 ml.), and triphenyl phosphite (4·6 g., 4·5 mmoles) were warmed on a water-bath to complete dissolution. On cooling, the tetrakis-ester crystallised. It was purified by recrystallization from benzene–hexane. Similarly, from tetrakis(triphenylphosphine)platinum and tri-(*p*-chlorophenyl phosphite)platinum, the compound $Pt[P(O{\cdot}C_6H_4{\cdot}Cl\text{-}p)_3]_4$, m. p. 165°, was obtained; mixed m. p. with (XXIII), 163°.

(XXIV) *Mono(tri*-p-*chlorophenylphosphine)tris(triphenyl phosphite)platinum*(0), $PtP(O{\cdot}C_6H_4{\cdot}Cl\text{-}p)_3[P(OPh)_3]_3$. $Pt[P(C_6H_4{\cdot}Cl\text{-}p)_3]_4$ (3·2 g., 1 mmole) and triphenyl phosphite (3·5 g., 4·5 mmoles) in ethanol (50 ml.) were kept on a water-bath until solution was complete. From the filtered solution, the pale yellow crystalline *complex* was obtained on cooling. It is very soluble in benzene and chloroform, much less soluble in ethanol (Found: Pt, 13·5; Cl, 7·2; P, 7·3. $C_{72}H_{57}O_9Cl_3P_4Pt$ requires Pt, 13·1; Cl, 7·1; P, 8·3%).

(XXV) *Mono(triphenylphosphine)tris(tri*-p-*chlorophenyl phosphite)platinum*(0). $Pt[P(C_6H_5)_3]_4$ (3·1 g., 1 mmole) and tri-*p*-chlorophenyl phosphite (3·1 g., 3 mmoles) in ethanol (50 ml.) were kept on a water-bath for about 1 hr. From the filtered solution the *compound* separated on cooling, as crystalline leaflets, soluble in cold benzene or chloroform and in warm ethanol (Found: Pt, 11·7; Cl, 18·6; P, 7·1. $C_{72}H_{51}O_9Cl_9P_4Pt$ requires Pt, 11·5; Cl, 18·7; P, 7·3%).

(F) *Reaction of Carbon Monoxide on the Compounds of Tetrakisarylphosphineplatinum*(0).—(XXVI) *Dicarbonylbis(triphenylphosphine)platinum*(0), $Pt(CO)_2(PPh_3)_2$. (*a*) This compound was obtained (mixed with 2 mol. of triphenylphosphine) when $Pt(PPh_3)_4$ was treated with carbon monoxide at 300 atm. The temperature has no effect in the range 20—90°, and the reaction at 20° is complete in about 12 hr. The product loses carbon monoxide slowly, becoming yellow. With all the solvents which dissolve the phosphine, evolution of carbon monoxide takes place. The mixture melted at 118° with gas evolution [same m. p. as that of $Pt(PPh_3)_4$] {Found: CO, 4·50. $Pt(CO)_2[PPh_3]_2,2PPh_3$ requires CO, 4·3%}.

(*b*) From $Pt(PPh_3)_3$ and CO under the same conditions a *product* (m. p. 130°) was obtained which gave 5·35% of CO on heating with phenyl *iso*cyanide [$Pt(CO)_2(PPh_3)_2,PPh_3$ requires CO, 5·37%].

(XXVII) *Monocarbonyltris(triphenylphosphine)platinum*(0). When the mixture obtained as (XXVI, *b*) was dissolved in 10 parts of diethyl ether a brisk evolution of gas took place; on precipitation with 20 parts of ethanol orange-red crystals were obtained; m. p. 130° [Found: Pt, 19·9; CO, 2·7; P, 9·0. $C_{54}H_{45}P_3Pt(CO)$ requires Pt, 19·5; CO, 2·8; P, 9·3%].

(XXVIII) *Dicarbonylbis(tri*-p-*chlorophosphine)platinum*(0), prepared similarly to (XXVI, *b*) from $Pt[P(C_6H_4{\cdot}Cl\text{-}p)_3]_3$ (XVIII), is a crystalline powder which slowly loses carbon monoxide, turning red. It dissolves in diethyl ether, giving off half of its carbon monoxide {Found (in the mixture): CO, 3·9. $Pt(CO)_2[P(C_6H_4{\cdot}Cl\text{-}p)_3]_2,P(C_6H_4Cl\text{-}p)_3$ requires CO, 4·2%}.

(XXIX) *Monocarbonylbis(tri*-p-*chlorophenylphosphine)platinum*(0). This *compound* was formed slowly from (XXVIII) (admixed with tri-*p*-chlorophenylphosphine) by loss of carbon monoxide. In fact, (XXVIII), a few days after being prepared, dissolves in diethyl ether without

effervescence. By concentration of this solution, $Pt(CO)(PPh_3)_2$ was obtained as golden-yellow crystals, m. p. 141°. The same *compound* was obtained by dissolution of the freshly prepared compound (XXVIII) in diethyl ether, in this case with evolution of carbon monoxide [Found: Pt, 20·9; CO, 2·9; P, 7·0. $C_{36}H_{24}Cl_6P_2Pt(CO)$ requires Pt, 20·5; CO, 2·9; P, 6·9%]

We are indebted to the Italian Research Council (CNR) for a grant.

ISTITUTO DI CHIMICA GENERALE DELLA UNIVERSITÀ,
MILANO, ITALY.

[*Received, December 12th*, 1957.]

---

469. *The Acid–Base Function in Non-aqueous Solution. Part I. The Equilibria between Mono-, Di-, or Tri-*n*-butylamine and 2 : 4-Dinitrophenol in Chlorobenzene.*

By JOHN W. BAYLES and A. CHETWYN.

The equilibria between mono-, di-, or tri-*n*-butylamine and 2 : 4-dinitrophenol in chlorobenzene have been shown to be of the form, $B + HA \rightleftharpoons BHA$, where B represents a butylamine and HA represents the nitrophenol. The equilibrium constants have been determined spectrophotometrically in the temperature range 20—60°, and expressed as changes in standard Gibbs free energies, enthalpies, and entropies.

With 2 : 4-dinitrophenol as the reference acid and chlorobenzene as solvent, the basic strengths of these amines fall in the order, mono- < di- < tri-*n*-butylamine, when $-\Delta G^\circ$ for the above reaction is taken as a measure of the basic strength. This order is different from that found in aqueous solution. The values of $-\Delta H^\circ$ for the reactions in chlorobenzene behave in the same way. The results indicate that solvation is a factor in determining the relative strengths of the butylamines in water, and that the steric requirements of the proton or of 2 : 4-dinitrophenol are not of major importance.

THOUGH accurate measurements on the thermodynamics of the acid–base function of amines in water and aqueous solvents have been made,[1,2] the information on this property in solvents other than water is still very inadequate, though there is some qualitative information about the chemical entities present in these solutions. Maryott [3] has shown that the complexes formed in benzene and dioxan by various alkylammonium picrates have large dipole moments (11—12 D), and that the distance of closest approach between the positive and the negative centres is about 4·5 Å, consistently with salt formation. Infrared studies [4] have demonstrated that if the concentrations of amine and carboxylic acid in carbon tetrachloride or chloroform are decreased below approximately 10^{-3}M, the equilibrium type changes from a complex one between associated species to the simple form:

$$B + HA \rightleftharpoons BHA \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

The structure of the compound BHA may be written as $^+BH \ldots A^-$ or B . . . HA according to whether the proton is or is not transferred. Barrow [5] has suggested that only with proton transfer is the reaction of true acid–base type. In carbon tetrachloride solutions containing a phenol or naphthol as proton-donor, and dioxan, acetone, methyl acetate, nitromethane, or acetanilide as acceptor, the infrared spectra [6] indicate however that the proton oscillates between two positions of minimum potential energy. Therefore it does

[1] Everett and Wynne-Jones, *Proc. Roy. Soc.*, 1941, *A*, **177**, 499.
[2] A. G. Evans and Hamann, *Trans. Faraday Soc.*, 1951, **47**, 34.
[3] Maryott, *J. Res. Nat. Bur. Stand.*, 1948, **41**, 1.
[4] Barrow and Yerger, *J. Amer. Chem. Soc.*, 1954, **76**, 5211; 1955, **77**, 4474, 6206.
[5] Barrow, *J. Amer. Chem. Soc.*, 1956, **78**, 5802.
[6] Nagakura and Sato, *J. Chem. Soc. Japan, Pure Chem. Sect.*, 1955, **7**, 1007.

XUM

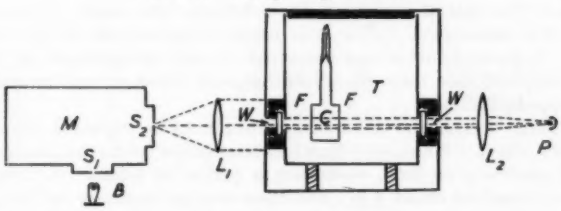
not seem possible to draw a sharp distinction between the above possibilities. Maryott's value [7] for the dipole moment of tribenzylammonium picrate in benzene is of the order to be expected for a molecule with charge separation, so in this system at least, there is strong evidence for proton transfer.

Bell and Bayles [8] have measured the equilibrium constants for the reactions between bromophenol-blue and various aromatic amines in chlorobenzene and anisole solution, and preliminary results were given for the system butylamine–2 : 6-dinitrophenol. The order of basic strength for the butylamines was found to be mono- < di- < tri-*n*-butylamine in chlorobenzene solution, and this order has also been found for the ethylamines [9] in ethanol–water or dioxan–water mixtures which are rich in the organic component. In the present work, the three amines, mono-, di-, and tri-*n*-butylamine, are studied in chlorobenzene solution, and for the first time both enthalpy and entropy changes are reported. In addition, some justification is attempted for the assumptions made in obtaining these thermodynamic quantities from the experimental measurements.

Experimental

Chemicals.—Chlorobenzene (B.D.H.) was first distilled. It was then fractionated, and the middle fraction was dried over fresh phosphoric oxide for 2—9 days. It was then re-fractionated, and the fraction distilling at 132° ± 0·5° was collected. An aqueous extract of a sample taken from every batch of chlorobenzene was tested with B.D.H. Universal indicator. If the pH of the extract differed from 7, the batch was discarded.

Fig. 1. *The spectrophotometer.*



2 : 4-Dinitrophenol was twice crystallized from alcohol, dried *in vacuo* (NaOH) for several days, and stored in a desiccator (P_2O_5): it had m. p. 112° (lit., 111·6°).

Mono-*n*-butylamine (B.D.H.) was dried (K_2CO_3) for 1 day, then fractionated, and the middle fraction, b. p. 77·0°, was collected. Di-*n*-butylamine (B.D.H.) was dried (NaOH) and then fractionated. The fraction of b. p. 158—159° was collected. Tri-*n*-butylamine (Imperial Chemical Industries Limited) was dried (KOH) for 15 days, and then fractionated. The fraction of b. p. 210—212° was collected. The purity of the three amines was checked by titration against standard acid.

Apparatus.—The glassware and optical cells were baked for at least 2 hr. at 150—170° before use, and left in a vacuum-desiccator over potassium hydroxide.

The Spectrophotometer.—The essential features of the spectrophotometer can be seen from Fig. 1. Light from a 30 w tungsten filament bulb, *B*, is passed through a Bellingham and Stanley direct-reading spectrometer, *M*, whose eyepiece has been replaced by a bilateral exit slit, S_2. The lens, L_1, collimates the monochromatic beam, which passes through one of four 2-litre thermostats, *T*, contained in a long rectangular trough running perpendicularly to the plane of the paper. The light is then focused on a photomultiplier tube, *P*, by the lens L_2. The thermostats are arranged to operate at approximately 30°, 37°, 47°, and 57° ± 0·05°. The sealed mercury–toluene regulators, stirrers, and glass-enclosed fish-tank heaters are not shown in the Figure. The tank windows, *W*, are of Perspex.

[7] Maryott, *J. Res. Nat. Bur. Stand.*, 1948, **41**, 7.
[8] Bell and Bayles, *J.*, 1952, 1518.
[9] Rumpf, Girault-Vexlearschi, and Schaal, *Bull. Soc. chim. France*, 1955, 554.

XUM

The bulb, monochromator, collimating and focusing lenses, and photomultiplier tube were mounted on a high-tensile light-alloy casting which itself was mounted on two parallel steel bars, not shown, along which it could slide freely. The light beam could therefore be passed through any one of the four thermostats.

The 1 cm. Pyrex cell, *C*, has a cylindrical body, optically flat fused-on end-faces, *F*, and a side-arm. These cells are completely immersed in the thermostat, and two equally good methods were used for closing them. One method is to attach a B7 cone to the side-arm and close it with a B7 cap, silicone grease being used. In the other the side-arm is drawn to a capillary, 3 cm. long by 1 mm. internal diameter, and then sealed in a flame after filling of the cell. Filling was achieved with an all-glass hypodermic syringe whose metal needle was replaced by a fused-on fine-glass capillary which could be inserted into the capillary side-arm of the cell. The comparison cell filled with solvent was prepared in the same way.

The method of measuring the optical density of a solution was similar to that used on commercial instruments. The instrumental uncertainty of measurements was $\pm 0{\cdot}002$ for optical density in the region of 50% transmission or 0·3 optical density. The way in which this uncertainty changes with measured optical density runs parallel to the behaviour of the well-known commercial instruments. The resolution of the instrument for sodium D light (width of line in mμ at half its maximum intensity) is 8·1 mμ for the slit-width used in this work.

Solutions.—Approximately 0·06 g. of 2 : 4-dinitrophenol was weighed out in a 50 ml. graduated flask, and chlorobenzene was added, its weight being found by difference. This solution was then diluted by weight to give a solution with a mole fraction of 2 : 4-dinitrophenol approximately ten times that required in the final solution. A solution of amine in chlorobenzene was made in a similar way.

The working solutions were obtained by weighing approximately the correct proportions of the 2 : 4-dinitrophenol and amine solutions, and finally diluting by weight with chlorobenzene to give a measurable optical density.

Measurements of the optical density of the solutions were made at room temperature on the Unicam S.P. 500 instrument, and at four higher temperatures on the spectrophotometer described above. A given solution was measured at each temperature in turn in increasing order of temperature, and then three more readings were taken at each temperature in random order to check reproducibility.

The reproducibility was of the order of magnitude to be expected from the intrumental uncertainties quoted above. Solutions which had been subjected to the procedure just described showed no visual tendency to fade, even over a period of weeks. A complete experiment on a given solution lasted for about 4 hr., and there was no tendency for the optical density to increase or decrease during this period. One solution having an optical density of 0·572 at 29·5° gave an identical reading 24 hr. later.

The above procedure was repeated for different mole fractions of amine and indicator, designed to cover the measurable range of optical densities. Fresh solutions were made up from time to time to eliminate possible errors in the various dilutions.

Results

Units.—The equilibrium constant applicable to this reaction is found experimentally (see below) to have the form:

$$K = [\mathrm{BHA}]/[\mathrm{HA}][\mathrm{B}] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

It is particularly convenient in the present work to express all concentrations as mole fractions and to calculate K in terms of these units. This is because mole fractions are independent of temperature, and so in the preparation of solutions no corrections for the considerable coefficient of expansion of chlorobenzene need be made.

The spectrophotometric determinations of the coloured complex BHA in equation (2) lead to the concentration, c, of the complex in mole $l.^{-1}$ if the ordinary extinction coefficient, ε_λ, is used in conjunction with the usual equation:

$$c = D_\lambda/\varepsilon_\lambda d \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where D is the optical density at wavelength λ, ε_λ is the molar extinction coefficient at wavelength λ, and d is the optical path length through the solution.

This value for c may then be expressed as a mole fraction, x, by using the relation, true for dilute solutions:

$$x = MD_\lambda/1000\rho_T\varepsilon_\lambda d$$

or, writing,

$$\varepsilon_{x,T,\lambda} = (1000\rho_T/M)\varepsilon_\lambda$$

then,

$$x = D_\lambda/\varepsilon_{x,T,\lambda}d \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

The subscripts, T and λ, are retained in the new quantity, $\varepsilon_{x,T,\lambda}$ to emphasize its dependence on temperature as well as wavelength.

In using the expression (4), the value of $\varepsilon_{x,T,\lambda}$ is plotted against temperature, and interpolated for the working solution concerned. The calculation of mole fractions is then analogous to that used in finding concentrations by using ε_λ.

Strictly, the expression for K is:

$$K = (x_{BHA}/x_B \cdot x_{HA})(\gamma_{BHA}/\gamma_B \cdot \gamma_{HA})$$

and values of the activity coefficients, γ, should be estimated. In the present work we assume that the quotient of activity coefficients is unity or constant. For the free amine and nitrophenol at low concentrations this is very probably a good assumption, and though the complex,

FIG. 2.

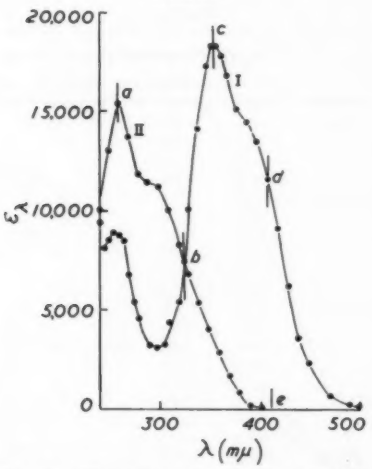


FIG. 3.

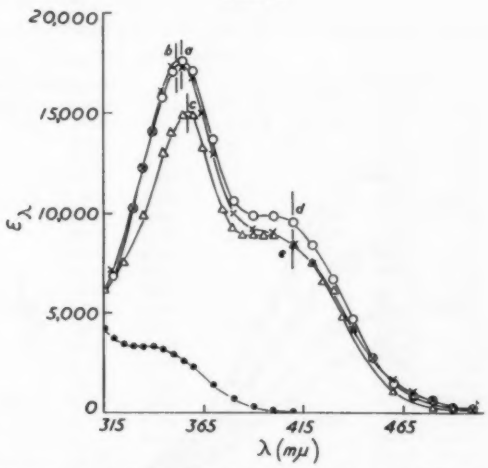


FIG. 2. *The spectra of basic* (I) *and acidic* (II) *aqueous solutions of* 2 : 4-*dinitrophenol.* $\lambda_a = 261$ mμ, $\varepsilon_a = 15{,}300$. $\lambda_b = 323$ mμ, $\varepsilon_b = 7350$. $\lambda_c = 357{\cdot}5$ mμ, $\varepsilon_c = 18{,}300$. $\lambda_d = \lambda_e = 410$ mμ, $\varepsilon_d = 11{,}600$; $\varepsilon_e = 0$. [2 : 4-$C_6H_3(NO_2)_2$·OH] = $5{\cdot}758 \times 10^{-5}$ mole l.$^{-1}$; [NaOH] in I = 0·1 mole l.$^{-1}$; [H_2SO_4] in II = 0·05 mole l.$^{-1}$.

FIG. 3. *Absorption spectra for* 2 : 4-*dinitrophenol in chlorobenzene solution in the presence of excess of chloroacetic acid,* ●; *mono*-n-*butylamine,* ○; *di*-n-*butylamine,* ×; *and tri*-n-*butylamine,* △. $\lambda_a = 355$ mμ, ε_a (for $Bu^n{\cdot}NH_2$) = 17,600. $\lambda_b = 352{\cdot}5$ mμ, ε_b (for Bu^n_2NH) = 17,400. $\lambda_c = 357{\cdot}5$ mμ, ε_c (for Bu^n_3N) = 15,000. $\lambda_d = \lambda_e = 410$ mμ, ε_d (for $Bu^n{\cdot}NH_2$) = 9600, ε_e (for Bu^n_2NH and Bu^n_3N) = 8400.

BHA, will have a relatively high dipole moment, at concentrations of the order 10^{-5} mole l.$^{-1}$ (mole fraction of the order 10^{-6}) we do not expect that dipole association will be sufficiently important to cause γ_{BHA} to depart very markedly from unity. The plots in Fig. 6 may also be taken as partial justification of the assumption.

Absorption Spectra.—2 : 4-Dinitrophenol in solution gives rise to two well-defined absorption spectra according to whether the solution contains an acidic or a basic component in addition to the 2 : 4-dinitrophenol. The spectra of acidic and basic solutions of 2 : 4-dinitrophenol in water are given in Fig. 2. These may be compared with the spectra of this substance in chlorobenzene solution to which chloroacetic acid or an amine has been added (Fig. 3).

XUM

The solutions whose spectra appear in Fig. 3 contained sufficient amine to effect complete conversion of the 2 : 4-dinitrophenol into its ionized form, and would correspond to points on

FIG. 4. *Apparent extinction coefficient of* 2 : 4-*dinitrophenol at* 410 mμ, $D_{410}/[C_6H_3(NO_2)_2{\cdot}OH]$, *in chlorobenzene solutions containing various concentrations,* c_B, *of amines.* [The added amine is mono-*n*-butylamine for ○, di-*n*-butylamine for ×, and tri-*n*-butylamine for ●. The limits of the apparent extinction coefficients are 9600, 8400, and 8400 respectively.]

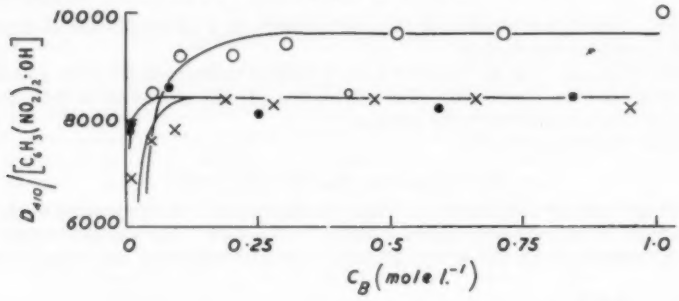


FIG. 6.

FIG. 5.

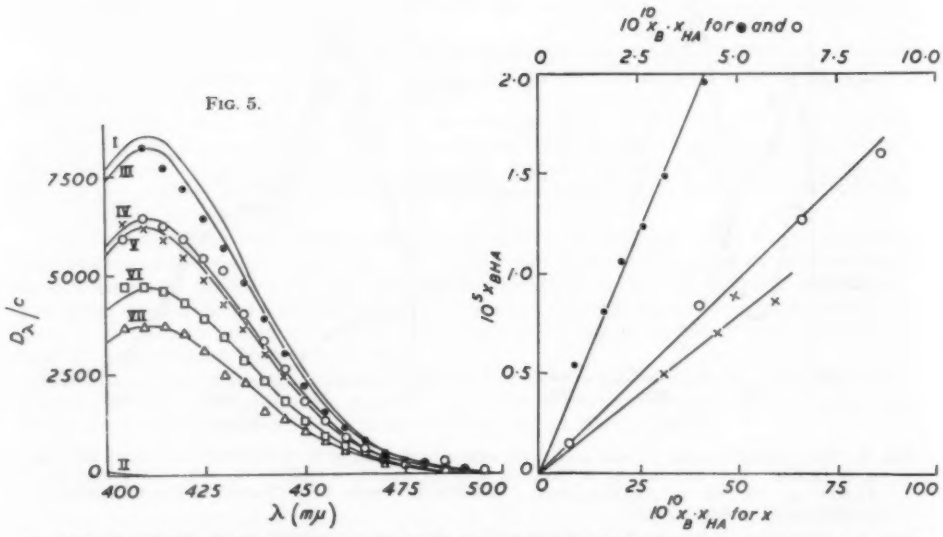


FIG. 5. *A solution of di-*n*-butylamine and* 2 : 4-*dinitrophenol at different temperatures: comparison of observed spectra (plotted points) with those calculated (full curves) from the spectra of the acid and basic forms of* 2 : 4-*dinitrophenol.*

I: *Spectrum of* 2 : 4-*dinitrophenol,* 100% *basic form, from Fig.* 3, *curve* ×. II: *Spectrum of* 2 : 4-*dinitrophenol,* 100% *acidic form, from Fig.* 3, *curve* ●. III: *Calc. for* 97·3% *basic form.* ●: *Experimental points at* 17·5°. IV: *Calc. for* 75·5% *basic form.* ○: *Experimental points at* 30·5°. V: *Calc. for* 73·2% *basic form.* ×: *Experimental points at* 35·5°. VI: *Calc. for* 55·7% *basic form.* □: *Experimental points at* 47·5°. VII: *Calc. for* 44·1% *basic form.* △: *Experimental points at* 57·5°.

FIG. 6. *Test of the equilibrium in chlorobenzene solution,* B + HA $\rightleftharpoons$ BHA, *in which* HA *is* 2 : 4-*dinitrophenol and* B *is mono-*n*-butylamine* (×), *di-*n*-butylamine* (○), *or tri-*n*-butylamine* (●). x_B, x_{HA}, *and* x_{BHA} *are mole fractions at equilibrium.*

the horizontal part of the curves in Fig. 4. It is seen that the wavelengths of maximum absorption, λ_a, λ_b, λ_c, in Fig. 5 agree very closely with the corresponding wavelength, λ_c, in Fig. 2. It seems justifiable therefore to suppose that in chlorobenzene solutions containing

XUM

2 : 4-dinitrophenol and amine in excess, the former is present in the ionized state. At 410 mμ the difference between the extinction coefficients of the acidic and the basic form is greatest, and this wavelength is therefore used in determinations of the relative amounts of each in equilibrium mixtures in the solvent. It is convenient that the acidic form of 2 : 4-dinitrophenol does not absorb at this wavelength.

Extinction Coefficients in Chlorobenzene Solution.—It was found that the apparent extinction coefficient of 2 : 4-dinitrophenol in the presence of mono-, di-, and tri-*n*-butylamine reached a limit as the concentration of amine in the solution was increased. This is shown in Fig. 4 where the values of the extinction coefficients at 410 mμ, ε_{410}, for the three amines at this limit are indicated.

The actual nitrophenol concentrations were varied in making up the solutions for Fig. 4. The same limit of extinction coefficient is reached whatever the nitrophenol concentration, and so Beer's law must be obeyed.

Variation of Absorption Spectrum with Temperature.—The calculation of ΔH for the reaction between 2 : 4-dinitrophenol and the butylamines depends on the assumption that, as the temperature changes in solutions containing these components, the resultant changes in absorption spectrum are due solely to an alteration in the relative concentrations of the species BHA and

TABLE 1. *Experimental results for the equilibria in chlorobenzene:*

$$2:4\text{-}(NO_2)_2C_6H_3\cdot OH + B \rightleftharpoons 2:4\text{-}(NO_2)_2C_6H_3\cdot O\cdot H\cdot B,$$

where X_B and X_I are the stoicheiometric mole fractions of B *and* 2 : 4*-dinitrophenol present in the equilibrium solutions. The values for D_{410} are mean values.*

Mono-*n*-butylamine				Di-*n*-butylamine				Tri-*n*-butylamine			
10^5X_B	10^5X_I	Temp.	D_{410}	10^5X_B	10^5X_I	Temp.	D_{410}	10^5X_B	10^5X_I	Temp.	D_{410}
145·9	0·711	19·0°	0·52	1·407	0·725	20·5°	0·17	2·968	3·616	18·0°	1·51
		20·5	0·50			30·0	0·09			19·5	1·44
		30·0	0·43			35·5	0·07			31·5	0·95
		35·5	0·37			47·0	0·04			36·5	0·80
		47·0	0·25	2·802	2·872	19·5	0·83			48·0	0·51
		57·0	0·16			20·0	0·85			57·5	0·34
241·7	1·095	19·0	0·91			30·0	0·58	5·785	1·803	21·0	1·12
		20·5	0·90			35·5	0·45			31·5	0·85
		30·0	0·77			47·0	0·27			36·5	0·73
		35·5	0·70			57·0	0·16			48·0	0·46
		47·0	0·56	3·667	5·750	18·5	1·60			57·5	0·30
		57·0	0·41			19·0	1·58	5·801	3·563	18·5	2·12
155·9	1·244	15·5	0·97			30·5	1·12			31·5	1·32
		18·0	0·95			35·5	0·97			36·5	1·22
		22·0	0·85			36·5	0·95			48·0	0·84
		24·5	0·79			47·0	0·62			57·0	0·56
		47·0	0·45			48·5	0·55	4·055	1·306	18·0	0·73
		57·0	0·28			57·0	0·39			18·5	0·75
115·3	1·087	21·1	0·678	6·375	2·564	22·8	1·078			19·0	0·78
		24·0	0·668			24·5	1·05			31·5	0·50
		29·5	0·587			37·0	0·710			36·5	0·44
		30·0	0·572			48·0	0·456			47·0	0·27
		47·1	0·305			56·7	0·310			57·5	0·19
		57·0	0·180					8·056	1·348	18·5	0·98
										19·5	0·98
										31·0	0·70
										36·5	0·63
										47·0	0·45
										57·0	0·29
								7·877	6·569	18·5	0·48
										19·5	0·46
										31·0	0·36
										36·5	0·32
										47·0	0·21
										57·0	0·14

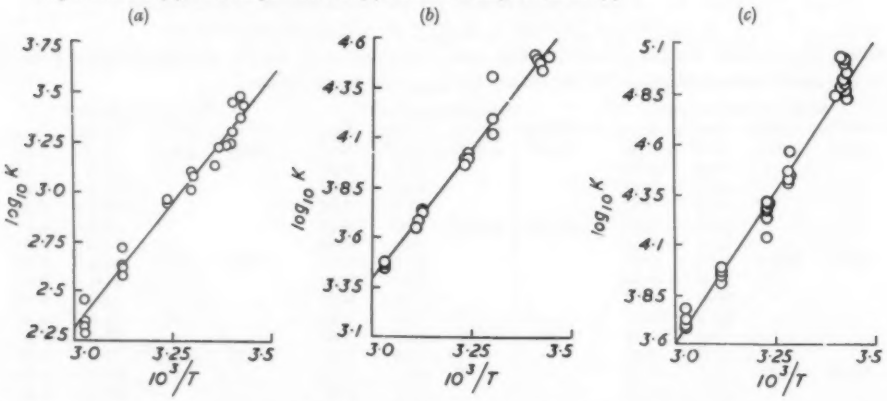
HA. The free amine does not absorb light in the spectral region concerned, so it remains necessary to show that no species are produced other than those accounted for by the chemical equation.

The point is partly met in Fig. 6 where the form of the equilibrium constant is demonstrated,

but, in addition, we mave measured the absorption spectra of a solution containing di-*n*-butylamine and 2 : 4-dinitrophenol over a range of temperature, and the results are plotted in Fig. 5. The reaction is exothermic and, as the temperature of the equilibrium mixture is increased, the characteristic absorption due to the ionized form of the nitrophenol decreases in intensity. This is due to displacement of the equilibrium (1) towards the reactant side. It is seen that the experimental points can be reproduced quantitatively by the curves, which have been calculated for the stated degrees of conversion of 2 : 4-dinitrophenol into its ionized form. If any light-absorbing species other than BHA of equation (1) were produced reversibly as the temperature increased, such agreement would not be expected. Any irreversible reaction would be detected by the method we have adopted for measuring the optical densities over a temperature range. This has been described under *Solutions*.

Form of K at Constant Temperature.—The optical density of solutions containing 2 : 4-dinitrophenol and amine was measured over a range of temperatures to yield the results reported below for the dependence of log K on temperature. The optical density of each solution was interpolated at 25° from these results, and expressed as mole fraction of complex, x_{BHA}. This

FIG. 7. *The relation between* $\log_{10} K$ *and* T^{-1}, *where* K *is the equilibrium constant (mole fraction scale) for the equilibrium,* B + HA $\rightleftharpoons$ BHA, *in which* HA *is* 2 : 4-*dinitrophenol, and* B *is mono-*n-*butylamine in* (*a*), *di-*n-*butylamine in* (*b*), *and tri-*n-*butylamine in* (*c*).



has been plotted against the product of the mole fractions of the 2 : 4-dinitrophenol and amine, $x_{HA} \cdot x_B$, in each corresponding solution at equilibrium, and yields the set of linear graphs shown in Fig. 6. This is evidence that the equilibrium constant is of the form,

$$K = x_{BHA}/x_B \cdot x_{HA}$$

and hence that (*a*) the equilibrium studied is of the type (1) and (*b*) the activity coefficient quotient either is unity or remains constant over the range of concentration used. The concentrations are so low that we consider it likely that the quotient is unity.

Variation of Equilibrium Constant with Temperature.—In Figs. 7*a*, *b*, *c*, are shown the graphs of log K against T^{-1} where the lines drawn are obtained by the method of least squares. The $\Delta G°$ values at 25° are calculated by interpolation, and $\Delta H°$ and $\Delta S°$ from the slope. The results obtained are presented in Table 2, in which the estimated probable errors (*i.e.*, 0·67 times the standard errors) are obtained by applying standard statistical procedures to the probable errors of the slopes and intercepts of the lines drawn in the Figures.

DISCUSSION

It is evident from Table 2 that if $-\Delta G°$ for the reaction (1) between a set of amines, B, and 2 : 4-dinitrophenol, HA, is taken as the measure of the strength of the bases, then for mono-, di-, and tri-*n*-butylamine the strengths in chlorobenzene increase in this order. This is in marked contrast to the behaviour of aliphatic amines in water,[1,2,10] and the

[10] N. F. Hall and Sprinkle, *J. Amer. Chem. Soc.*, 1932, **54**, 3469.

simplest interpretation, following Trotman-Dickenson,[11] is that in aqueous solution solvation of the aminium ions is greater for those ions carrying the most hydrogen atoms and the fewest alkyl groups. The solvation of the ions is also assumed to be greater than that of the free amines in solution. The basic strengths in chlorobenzene increase in the manner predicted by the known inductive effect of the alkyl groups, leading to an increase of the electron-density on the nitrogen atom with the number of alkyl groups attached. We notice that in both chlorobenzene and aqueous solution the enthalpy changes are high and negative, indicating proton-transfer, and that they could lie in the sequence which would result if the energy of reaction in both solvents were largely determined by the electron-density on the nitrogen atom. Hence it seems that the contribution of solvation energies to the $\Delta H°$ values in water and in chlorobenzene is small. The entropies of solvation however will depend, not directly on the strength of binding of the solvation shells, but on their influence on the freedom of movement of the interacting entities. The $\Delta S°$ values for the reaction between mono-, di-, and trimethylamine and the hydroxonium ion in water are [1] 4·7, 9·5, and 15·2 cal. deg.$^{-1}$ mole^{-1}, and, because the equilibrium is of the type, $AH + B \rightleftharpoons A^- + BH^+$, these values

TABLE 2. *Thermodynamic functions for the equilibria at 25° in chlorobenzene*: $2:4\text{-}(NO_2)_2C_6H_3\cdot OH + B \rightleftharpoons 2:4\text{-}(NO_2)_2C_6H_3\cdot O\cdot H\cdot B$.

Amine, B	$10^{-3}\partial \log_{10} K/\partial T^{-1}$	log K	$\Delta G°$ (kcal. mole^{-1})	$\Delta H°$ (kcal. mole^{-1})	$\Delta S°$ (cal. deg.$^{-1}$ mole^{-1})
$Bu^n\cdot NH_2$ ...	2·64 ± 0·06	3·23 ± 0·24	−4·39 ± 0·33	−12·1 ± 0·3	−25·8 ± 1·5
Bu^n_2NH ...	2·56 ± 0·03	4·31 ± 0·12	−5·87 ± 0·16	−11·7 ± 0·2	−19·7 ± 0·7
Bu^n_3N	3·09 ± 0·05	4·68 ± 0·19	−6·37 ± 0·26	−14·1 ± 0·2	−26·0 ± 1·2

do not depend on the concentration scale chosen. The roughly constant difference of 4 cal. deg.$^{-1}$ mole^{-1} in these equilibria has been ascribed to the effect of solvation.[2] In chlorobenzene solutions of the butylamines, values of $\Delta S°$ for the reaction (1) (mole fraction units being used) are large and negative (Table 2). The three values all lie within a range of 4·5 cal. deg.$^{-1}$ mole^{-1}, which is only just outside the limits of experimental error, and there is no consistent change from mono- to di- to tri-*n*-butylamine.

Brown [12] has suggested that competition between inductive and steric factors accounts for the low basic strengths of 2 : 6-di-*tert.*-butylpyridine, and possibly of *o*-methyl- and *o*-*tert.*-butyl-aniline. If steric factors were of importance in determining the basic strengths of the butylamines, the effect should be greater in the present systems in chlorobenzene where there is association with 2 : 4-dinitrophenol, than in water where dissociation takes place. If steric factors predominated, tributylamine would therefore be even weaker in relation to mono- and di-butylamine in chlorobenzene as solvent than it is in water. The fact that we find the reverse indicates that steric factors are not of determining importance in the systems discussed in the present work.

The results of Hall [13] on the electromotive force of cells containing a wide variety of bases in various organic solvents led to the conclusion that solvation effects " are not important enough to cause major disturbances in the order of base strengths " in non-aqueous solvent as compared with the order in water. The present work demonstrates that, though the effect may be small in comparison with that of major structural changes in the molecule, it is more important than the simple inductive effect accompanying the exchange of a hydrogen atom for an alkyl group on a nitrogen atom.

We thank Imperial Chemical Industries Limited for the loan of the Bellingham and Stanley direct-reading spectroscope used in the construction of the spectrophotometer, and for some chemicals. One of us (A. C.) thanks University College, Cardiff, for the award of a British Nylon Spinners Scholarship.

UNIVERSITY COLLEGE, CARDIFF. [*Received, October 18th*, 1957.]

[11] Trotman-Dickenson, *J.*, 1949, 1293.
[12] Brown, *J.*, 1956, 1248.
[13] H. K. Hall, *J. Phys. Chem.*, 1956, **60**, 63.

470. *Substituted Benzidines and Related Compounds as Reagents in Analytical Chemistry. Part XIV.* 3-Bromo- and 3 : 3′-Dibromobenzidine as Redox Indicators.*

By R. Belcher, A. J. Nutten, and W. I. Stephen.

3-Bromo- and 3 : 3-dibromo-benzidine undergo reversible oxidation in inorganic redox systems. These compounds can be used as redox indicators in the titration of iron(II) with potassium dichromate and with ceric sulphate. Sharp end-points (colourless to yellow) are obtained.

It has been suggested that, in the benzidine series, meriquinonoid salts stable to further and irreversible oxidation could probably only be obtained by *N*-alkylation.[1] Although the properties of nuclear alkyl-substituted benzidines do not differ greatly from those of the parent diamine [2] we now find that substitution by chlorine or bromine in the 3- and 3 : 3′-positions (but not in the 2- or 2 : 2′-positions) gives products with many oxidising agents which are highly coloured and more stable than those given by the parent diamine. The present study describes the behaviour of these four halogenated benzidines in conventional inorganic redox systems, and an assessment of their value as redox indicators.

All four compounds undergo the reactions characteristic of benzidine. In dilute acetic acid, the colours vary from blue-green for the monosubstituted to green for the disubstituted compounds, all changing to bright yellow or orange-yellow on the addition of dilute mineral acid. Similar yellow products are obtained by direct oxidation of the compounds in dilute mineral acid; the only difference observed is that the bromo-derivatives give a more orange-yellow colour than the chloro-derivatives which are oxidised to bright canary-yellow products. The colours which appear in dilute acetic acid are not very stable and fade in 10—15 minutes, but those formed in mineral acid only gradually decrease in intensity.

The oxidation of these halogenated benzidines in aqueous solutions is reversible. With the majority of simple benzidine derivatives, this process is too slow to allow of their use as indicators in redox titrimetry; only one such compound, *o*-dianisidine (3 : 3′-dimethoxybenzidine), has been used to any extent as a redox indicator. The halogenated benzidines, however, showed a sufficiently sharp colour change in solution to warrant their application for this purpose. When they were used in the titration of iron(II) with potassium dichromate and ceric sulphate all four behaved reversibly, but only 3-bromo- and 3 : 3′-dibromo-benzidine gave sharp enough end-points to have practical applications. 3-Chloro- and 3 : 3′-dichloro-benzidine reacted sluggishly and although end-points could be detected quite readily the titrant had to be added very slowly in the region of the end-point to allow time for the indicator reaction. The bromo-derivatives on the other hand responded instantly to the addition of either the oxidant or the reductant, and the colour change at the end-point could be obtained many times without apparent destruction of the organic compounds. At elevated temperatures, the indicator reaction still occurs, but is accompanied by some destruction of the reversibly formed oxidation products.

The transition potentials of 3-bromo- and 3 : 3′-dibromo-benzidine have been determined, the apparatus and procedure described previously [3] being used, and the results for each indicator over a range of acid concentrations are tabulated. These potentials lie midway between the accepted values for diphenylamine-4-sulphonic acid and tris-(1 : 10-phenanthroline) ferrous sulphate (840 and 1080 mv, respectively in M-sulphuric acid). Potentiometric studies of the ferrous–dichromate and ferrous–ceric titrations show that

* Part XIII, *J.*, 1954, 2543.

[1] Belcher, Nutten, and Stephen, *J.*, 1954, 2543.
[2] Belcher and Nutten, *J.*, 1951, 546.
[3] *Idem*, *J.*, 1952, 3857.

XUM

both bromobenzidine indicators function in the potential range over which the end-points of these titrations occur.

Transition potentials (mV, *referred to the hydrogen electrode*) *of* 3-*bromo- and* 3 : 3′-*dibromo-benzidine in various concentrations of sulphuric acid at* 18°.

	3-*Bromobenzidine*					3 : 3′-*Dibromobenzidine*				
Acid concn. (M) ...	0·5	1·0	2·0	4·0	8·0	0·5	1·0	2·0	4·0	8·0
E.M.F. (mv)	892	900	912	920	—	920	936	954	960	965

No simple benzidine derivative has been found which has a transition potential as high as those of the bromo-derivatives. Only one other substance, *N*-phenylanthranilic acid (diphenylamine-2-carboxylic acid) which depends on coloured meriquinonoid oxidation products for its use as a redox indicator, is reported [4] as having a similarly high transition potential (1080 mv) (our preliminary observations on this indicator point to a transition potential much nearer to that of the bromobenzidines).

In titrations of iron(II) solutions with both potassium dichromate and ceric sulphate, the dibromo-derivative gives the sharper end-point, this difference becoming more noticeable as the acidity of the solution is increased above the optimum acidity of 2M for both indicators. In the iron(II)–dichromate titration, it is unnecessary to add phosphoric acid. Titrations in hydrochloric acid are unsatisfactory because at the end-point the yellow colour of the ferric chloride obscures the colours of the oxidised indicators.

Both indicators function well in solutions warmed to 60°, which suggested their use in the direct titration of oxalic acid with ceric sulphate. It was found, however, that the indicators themselves were oxidised beyond the meriquinonoid stage, even when they were added near the equivalence point of the titration. Satisfactory end-points were only obtained in the presence of large amounts of indicator which, in turn, gave rise to high results for the titration.

Results for the titration of iron(II) with 0·1N-ceric sulphate and 0·1N-potassium dichromate showed good agreement (±0·02%) between the experimental and the theoretical titres.

Methods for the preparation of 3 : 3′-dichloro- and 3 : 3′-dibromo-benzidine are reported in the literature. Cohn [5] obtained 3 : 3′-dichlorobenzidine by the reduction of *o*-chloronitrobenzene with zinc dust and alkali; Synder, Weaver and Marshall [6] used a similar reaction for the preparation of 3 : 3′-dibromobenzidine. We prefer to use the procedure described by the latter workers for the preparation of the dichloro-derivative also. Only a procedure involving the condensation of *o*-chloro- or *o*-bromo-aniline with nitrosobenzene proved satisfactory for the preparation of the appropriate azo-compound leading to 3-chloro- or 3-bromo-benzidine. Bamberger [7] mentioned this reaction for the preparation of 3-chloro- and 3-bromo-azobenzene, but he gave no experimental details. 2-Chloro- and 2-bromo-azobenzene so obtained were reduced with zinc dust and alkali, and the hydrazo-compounds then rearranged to the required benzidines.

Experimental

Determination of the Transition Potentials of 3-*Bromo- and* 3 : 3′-*Dibromo-benzidine.*—The previously described [3] apparatus and procedure were used.

Solutions required: [3] Potassium dichromate, 0·1N. Ceric sulphate, 0·1N. Ferrous ammonium sulphate, 0·1N. Sulphuric acid, 2M.

Indicator solutions. 3-Bromo- or 3 : 3′-dibromo-benzidine (0·2 g.) was dissolved in warm glacial acetic acid (100 ml.).

[4] Syrokomsky and Stiepin, *J. Amer. Chem. Soc.*, 1936, **58**, 928.
[5] Cohn, *Ber.*, 1900, **33**, 3552.
[6] Snyder, Weaver, and Marshall, *J. Amer. Chem. Soc.*, 1949, **71**, 289.
[7] Bamberger, *Ber.*, 1900, **33**, 3190.

Titration of Iron(II).—The iron(II) solution (5—25 ml.) was diluted to 100 ml. with 2M-sulphuric acid, and four drops of indicator were added. Potassium dichromate was run in from a burette, rapidly at first, then more slowly as the end-point was approached. The addition of dichromate was continued dropwise with shaking until a permanent colour change to yellow was obtained.

The same procedure was followed with ceric sulphate as the titrant.

Preparation of the Amines.—**3 : 3′-*Dichlorobenzidine*.** The procedure of Snyder, Weaver, and Marshall was followed, with the appropriate amount of *o*-chloronitrobenzene in place of *o*-bromonitrobenzene. The yield of 3 : 3′-dichlorobenzidine dihydrochloride was 40%. The free base, recrystallised from light petroleum (b. p. 60—80°), had m. p. 133°.

3-*Chlorobenzidine*. To nitrosobenzene (10·5 g.) in glacial acetic acid (30 ml.), *o*-chloroaniline (15 g.) in the same solvent (20 ml.) was added. The mixture was left overnight, then poured into *ca.* 1 l. of water. Alkali was added until the solution was almost neutralised, the remaining acid being removed with sodium carbonate. The mixture was extracted with ether, and the ethereal solution treated with ethereal hydrogen chloride. The precipitate of *o*-chloroaniline hydrochloride was filtered off, and the filtrate evaporated to about 100 ml. This solution containing 2-chloroazobenzene was subjected to column chromatography on alumina, the azo-compound being eluted with ether. The eluate was evaporated and the remaining red oil was cooled in ethanol–solid carbon dioxide. The crystalline mass was allowed to warm to 0° and the crystals were rapidly filtered off. This process of cooling, warming, and filtering was repeated with the oily residues until most of the azo-compound was obtained crystalline. The *2-chloroazobenzene* (45%) had m. p. 33° (Found: C, 66·6; H, 4·0; N, 12·9; Cl, 16·6. $C_{12}H_9N_2Cl$ requires C, 66·5; H, 4·2; N, 13·0; Cl, 16·4%).

2-Chloroazobenzene (5·5 g.) was dissolved in ethanol (50 ml.), and zinc dust (3·5 g.) was stirred into the mixture. A solution of sodium hydroxide (4 g. in a few ml. of water, made up to 50 ml. with ethanol) was added, the whole was boiled under reflux until the red colour had disappeared (after about 45 min.), then filtered into an excess of concentrated hydrochloric acid, and the residue of zinc oxide was washed with warm ethanol, the washings being added to the main bulk of filtrate. 3-Chlorobenzidine hydrochloride was precipitated from the filtrate and was recrystallised from dilute hydrochloric acid (yield, 5 g., 66%). The free *base* recrystallised from light petroleum (b. p. 40—60°) as needles, m. p. 75° (Found: C, 66·1; H, 5·2; N, 12·8; Cl, 16·1. $C_{12}H_{11}N_2Cl$ requires C, 65·9; H, 5·1; N, 12·8; Cl, 16·2%).

3-*Bromobenzidine*. The same procedure was followed, with 20 g. of *o*-bromoaniline in place of *o*-chloroaniline. *2-Bromoazobenzene* was obtained as red crystals, m. p. 36° (30%) (Found: N, 10·7; Br, 30·5. $C_{12}H_9N_2Br$ requires N, 10·7; Br, 30·6%). This (7·5 g.) was reduced as was the 2-chloro-compound (2 hours' reflux). 3-Bromobenzidine dihydrochloride was obtained in 50% yield. The *base* recrystallised from light petroleum (b. p. 40—60°) as needles, m. p. 81° (Found: N, 10·5; Br, 32·7. $C_{12}H_{11}N_2Br$ requires N, 10·7; Br, 32·9%).

CHEMISTRY DEPARTMENT, THE UNIVERSITY,
EDGBASTON, BIRMINGHAM, 15.

[*Received, January 30th*, 1958.]

XUM

471. *The Structure of Molecular Compounds. Part XII.* Molecular Compounds of Tri-o-thymotide.*

By D. Lawton and H. M. Powell.

Tri-*o*-thymotide forms molecular inclusion compounds with many substances such as alkanes and their derivatives including alkyl halides, alcohols, esters, ketones, ethers, and polymethylene dihalides. If the included molecule does not differ much from the " straight " chain type, the resulting compound belongs to one of two classes. A clathrate type, $2C_{33}H_{36}O_6,M$, is formed with included molecules, M, of greatest length less than 9·5 Å. Longer molecules are enclosed in a different channel-type structure of composition $C_{33}H_{36}O_6,xM$ where x, which need not be rational, diminishes with increasing length of the included molecule. Several ordered and disordered variations of the two structures have been found. Some of the channel structures give one-dimensional diffraction patterns, due to included molecules, superposed on the main single-crystal *X*-ray diffraction pattern. The unit-cell dimensions of the clathrate type increase slightly and in a regular manner to accommodate the larger included molecules. For the channel type the cell dimensions are more nearly constant but vary in a periodic way as the length of included molecules increases. These changes are explained. Each of the 50 compounds studied is a new example of spontaneous optical resolution.

In several sets of crystalline molecular compounds one component forms an enclosing structure around the other. For each series this structure has, with small variations, a fixed form maintained by strong bonding between its components. Thus in the β-quinol clathrates $3C_6H_4(OH)_2,M$ (where M = various small atoms or molecules),[1] and in the adducts of urea or thiourea with numerous aliphatic compounds [2] there are covalencies, hydrogen bonds, or other forms of strong interaction binding the atoms of the enclosing structure. The enclosable molecules are limited to those which can fit into the restricted spaces.

In some circumstances a number of different structures might be formed by a given enclosing component. Thus for the gas hydrates various forms of polyhedra of water molecules surrounding the hydrating molecules have been suggested.[3] Although water or a more complex molecule may in this way form several different enclosures the number will be limited by factors such as the positions of the hydrogen-bonded atoms and the number and direction of their links.

However, in certain instances van der Waals forces alone are sufficient to hold together the molecules of an enclosing structure. In such a case a greater adaptability to the shape of enclosed molecules is to be expected. The van der Waals equilibrium distances between neighbouring atoms vary more than the length of a given type of hydrogen bond, such as that between two phenolic hydroxyl groups. Also van der Waals attraction is not restricted, as is hydrogen bonding, either to particular atoms which have definite positions in the molecule or to special directions in space relative to the rest of the molecule. The interaction between enclosed and enclosing molecules is qualitatively similar to that between any two molecules ot the enclosing structure. The arrangements of the cage-forming molecules may therefore be considerably influenced by their interaction with the enclosed component.

* Part XI, *J.*, 1956, 4855.

[1] Palin and Powell, *J.*, 1948, 815.
[2] Schlenk, *Annalen*, 1949, **565**, 204; 1951, **573**, 142.
[3] Von Stackelberg, *Naturwiss.*, 1949, **36**; Clausen, *J. Chem. Phys.*, 1951, **19**, 259, 662; Pauling and Marsh, *Proc. Nat. Acad. Sci.*, 1952, **38**, 112.

XUM

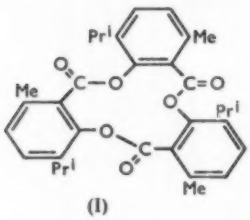
TABLE 1. *Adducts of tri-o-thymotide with unbranched molecules.*

Included molecule (A) R·OH, where R =	Calc. length of included molecule in extended form (Å)	Temp.	Dimensions of unit cell or pseudo-unit cell (ψ) (Å) a	c	Structure types apparent space-group		Density (g./c.c. at 20°)	No. of included molecules per unit cell containing 6 tri-o-thymotide molecules † Calc. from cell dimensions and density	By chemical analysis (approx.)
CH_3	4·6	18°	(13·460 ± 0·001) *	(30·223 ± 0·005) *	Cavity	$P3_121$	—	—	3
C_2H_5	5·6	6	—	30·136 ± 0·004	,,	,,	1·1627 ± 0·0005	3·03 ± 0·05	3·7
	—	7	13·440 ± 0·002	—					
	—	18	—	30·155 ± 0·001					
	—	19·5	13·455 ± 0·002	—					
	—	37·5	—	30·189 ± 0·003	—				
	—	38·5	13·470 ± 0·002	—					
C_3H_7	6·9	18	13·515 ± 0·003	30·288 ± 0·004	Cavity	$P3_121$	1·1606 ± 0·0005	2·98 ± 0·06	3·4
C_4H_9	8·1	18	13·617 ± 0·004 ψ	30·603 ± 0·004	,,	,,	1·1456 ± 0·0005	2·98 ± 0·05	3·5
C_5H_{11}	9·4	18	13·695 ± 0·006	30·742 ± 0·005	,,	,,	1·138 ± 0·002	2·9 ± 0·1	—
C_5H_{11}	9·4	18	14·310 ± 0·001	28·987 ± 0·002	Channel	$P6_3$	—	—	2·4
C_6H_{13}	10·7	19·5	14·268 ± 0·001	29·159 ± 0·003	,,	,,	1·1238 ± 0·0005	3·02 ± 0·03	3·1
C_7H_{15}	11·9	18	14·31 ± 0·01	29·055 ± 0·006	,,	$P6_1$	1·1217 ± 0·0005	2·67 ± 0·06	2·4
C_8H_{17}	13·2	19	14·307 ± 0·002	29·033 ± 0·002	,,	,,	1·1184 ± 0·0005	2·28 ± 0·02	2·4
$C_{10}H_{21}$	15·7	18	14·2825 ± 0·0005	29·120 ± 0·002	,,	,,	1·1251 ± 0·0005	2·00 ± 0·01	2·9
$C_{12}H_{25}$	18·2	18	14·314 ± 0·001	29·012 ± 0·006	,,	,,	1·1231 ± 0·0005	1·68 ± 0·02	—
$C_{16}H_{33}$	23·2	18·5	14·302 ± 0·001	29·050 ± 0·002	,,	,,	1·1263 ± 0·0005	1·32 ± 0·01	—
$C_{18}H_{37}$	25·7	18	14·304 ± 0·001	29·060 ± 0·005	,,	,,	1·1263 ± 0·0005	1·19 ± 0·01	—
(B) R·X									
R X									
CH_3 Br	5·9	—	13·467 ± 0·003	30·119 ± 0·005	Cavity	$P3_121$	—	—	2·6
CH_3 I	6·3	—	13·5	30·2	,,	,,	1·2597 ± 0·0006	*ca.* 3	—
C_2H_5 Br	6·8	—	13·540 ± 0·002	30·140 ± 0·002	,,	,,	1·2152 ± 0·0006	3·05 ± 0·02	3·0
C_2H_5 I	7·1	—	13·564 ± 0·005	30·28 ± 0·01	,,	,,	1·250 ± 0·002	2·96	2·9
C_3H_7 Br (A)	8·0	—	13·7 ψ	—	,,	,,	—	—	—
C_3H_7 Br (B)	8·0	—	13·62 ± 0·01 × 2	30·49 ± 0·03	,,	,,	1·206 ± 0·001	*ca.* 3	—
C_3H_7 I	8·4	—	13·7 × 2	30·3	,,	,,	1·2368 ± 0·0005	*ca.* 3	3·0
C_4H_9 Br	9·3	—	13·8 × 2	30·4	,,	,,	1·1908 ± 0·0003	*ca.* 3	2·7
C_4H_9 I	9·6	18	14·252 ± 0·003	29·030 ± 0·005	Channel	$P3_1$	1·207 ± 0·001	2·95 ± 0·03	2·4
C_5H_{11} Br	10·5	20·5	14·255 ± 0·001	29·137 ± 0·004	,,	,,	1·1747 ± 0·001	3·02 ± 0·03	2·6
C_5H_{11} I	10·9	*ca.* 18	14·288 ± 0·003	29·127 ± 0·006	,,	,,	1·2155 ± 0·0005	3·03 ± 0·02	3·1
C_6H_{13} Br	11·8	19	14·309 ± 0·001	29·120 ± 0·004	,,	$P6_1$	1·1650 ± 0·006	2·74 ± 0·12	2·6

C_7H_{15}	Br	13·0	16·5	14·323 ± 0·008	29·033 ± 0·003	,,	,,	1·1586 ± 0·0006	2·40 ± 0·04	2·5
		—	31·5	14·348 ± 0·006	29·024 ± 0·004	—		—	—	—
C_7H_{15}	I	13·4	18·5	14·321 ± 0·003	29·030 ± 0·005	,,	,,	1·1972 ± 0·0003	2·42 ± 0·02	2·1
C_8H_{17}	Br	14·3	19	14·294 ± 0·008	29·034 ± 0·008	,,	,,	1·1584 ± 0·0008	2·14 ± 0·04	1·96
C_8H_{17}	I (A)	14·7	—	14·3	29·0	,,	,,	—	—	2·2
C_8H_{17}	I (B)	14·7	18	14·278 ± 0·003 ϕ	29·024 ± 0·006	,,	,,	1·1791 ± 0·001	1·95 ± 0·02	2·1
$C_{16}H_{33}$	Br	24·4	16·5	14·311 ± 0·003	29·039 ± 0·002	,,	,,	1·1555 ± 0·001	1·36 ± 0·02	1·5
$C_{16}H_{33}$	I	24·7	19	14·306 ± 0·003	29·056 ± 0·009	,,	,,	1·1298 ± 0·004	0·95 ± 0·04	1·3
$C_{18}H_{37}$	Br	26·9	18	14·322 ± 0·001	29·078 ± 0·002	,,	,,	1·1540 ± 0·001	1·26 ± 0·01	—
$C_{18}H_{37}$	I (A)	27·2	20	14·320 ± 0·002	29·044 ± 0·008	,,	,,	1·1664 ± 0·001	1·19 ± 0·01	—
$C_{18}H_{37}$	I (B)	27·2	—	14·35 ± 0·05	29·2 ± 0·1		,,	1·144 ± 0·001	—	—
(C) $X\cdot[CH_2]_n\cdot X$										
n	X									
1	Br	7·0	21	13·537 ± 0·001 ϕ	30·174 ± 0·004	Cavity	$P3_121$	1·285 ± 0·004	3·07 ± 0·07	2·3
1	I	7·7	—	13·655 ± 0·005	30·33 ± 0·01	,,	,,	1·347 ± 0·001	2·99 ± 0·03	3
2	Br	8·3	—	13·7	30·3	,,	,,	—	—	2·6
3	Br (A)	9·5	—	13·9 ± 0·2	30·6 ± 0·3	,,	,,	—	—	1·2
3	Br (B)	9·5	—	13·79 ± 0·01 × 2	30·57 ± 0·02	,,	,,	—	—	3·1
6	I	14·0	—	14·2	29·2	Channel	$P6_1$	—	—	—
(D) ROR′										
R	R′									
C_2H_5	C_2H_5	8·9	18	13·623 ± 0·002	30·715 ± 0·010	Cavity	$P3_121$	1·1408 ± 0·001	3·03 ± 0·04	—
CH_3	C_4H_9	10·1	19	14·232 ± 0·002	29·153 ± 0·002	Channel	$P3_1$	1·117 ± 0·001	3·05 ± 0·05	—
C_2H_5	C_4H_9	11·4	18	14·252 ± 0·002	29·268 ± 0·002	,,	$P6_2$	1·1216 ± 0·0007	3·00 ± 0·03	—
(E) C_nH_{2n+2}										
C_6H_{12}		9·0	—	14·31 ± 0·05	29·05 ± 0·05	Channel	$P6_1$	—	—	—
C_6H_{14}		10·3	—	14·31 ± 0·05	29·05 ± 0·05	,,	$P3_1$	—	—	—
(F)										
I_2		7·0	—	13·33 ± 0·05	30·2 ± 0·3	Cavity	$P3_121$	1·33 ± 0·01	—	—
$Hg(C_2H_5)_2$		9·8	—	14·17 ± 0·04	29·06 ± 0·08	Channel	$P6_2$	—	—	—
(G)										
$C_2H_4I_2$. 90% of cavities vacant		—	—	13·35	30·12	Cavity	$P3_121$	1·185	—	—

* Product may be impure. The pure compound probably unobtainable. See text. † Given only when the constants are all known with sufficient accuracy.

Among compounds of this kind now discovered are the crystalline adducts of tri-*o*-thymotide (I) with a variety of substances. Wilson Baker, Gilbert, and Ollis [4] first showed the existence of such compounds. Two structures have already been recognised,[5] one containing benzene or chloroform and the other *n*-hexane. The two types although related in cell dimensions and in their symmetries are readily distinguishable. Many of the new adducts described in this paper have structures similar to one or other of them; some have structures which differ from both but have a structural relation to them, but in others no connection is apparent. This communication gives details only for those which are trigonal or hexagonal. These all resemble the two types mentioned but the symmetry relations prove to be complex and the two kinds cannot be contrasted simply by attributing to each a single space-group. For convenience they will be called the cavity and the channel type.



(I)

The cavity type includes adducts which resemble those of chloroform or benzene. They are trigonal and have $000l$ absent unless $l = 3n$. In general the *X*-ray reflection $hkil$ is not equal in intensity to $hki\bar{l}$, *i.e.*, oscillation photographs about the *c* axis are unsymmetrical above and below the zero layer-line, but those in which oscillation is about the *a* axis are symmetrical. The space-group is $P3_121$ (or enantiomorphous $P3_221$). The unit cell, referred to hexagonal axes, has *a* in the range 13·3—13·9 and *c* in the range 30·1—31·1 Å. This cell contains six molecules of tri-*o*-thymotide which by symmetry are all of the same enantiomorphous form. In nearly every case there are three molecules of the second component per unit cell; exceptionally a departure from the exact 2 : 1 ratio of tri-*o*-thymotide to the other component occurs.

The channel-type adducts are like that of *n*-hexane. The unit cells all have *a* about 14·3 and *c* about 29·0, *i.e.*, *a* is larger and *c* smaller than the corresponding dimension of the cavity type. On the basis of absent *X*-ray reflections they cannot all be attributed to the same space-group. Some, such as the *n*-pentyl alcohol adduct with $000l$ absent for $l \neq 3n$, appear to have space-group $P6_2$ (or enantiomorphous $P6_4$). For this space-group single-crystal oscillation photographs about the *c* axis should be symmetrical above and below the zero layer line, and should repeat every 60°. Close examination of the diffraction patterns shows that the *n*-pentyl iodide and some other adducts depart from this symmetry. Repetition occurs every 120° for oscillation about the *c* axis; oscillation photographs taken at 60° to each other have top and bottom interchanged. The effect is visible in only a few spots. Re-examination of the hexane adduct photographs, consequent on this observation, revealed similar but very faint effects. Differences of intensities of corresponding spots above and below the zero layer are slight, but that they are real symmetry effects is shown by the systematic alternations above and below the zero layer at 60° intervals. Accordingly for certain adducts the formal space-group will be $P3_1$ (or enantiomorphous $P3_2$). Since the effect in adducts of *n*-pentyl iodide and the molecules which contain a heavy atom is more marked than in *n*-hexane and other molecules which do not, it must be due to the included molecule. Others of these channel-type adducts with $000l$ absent when $l \neq 6n$ have space-group $P6_1$ (or enantiomorphous $P6_5$). Their oscillation photographs repeat accurately at 60° intervals around the *c* axis and are symmetrical about the zero layer.

Table 1(A) records constants for adducts with a series of *n*-alcohols. The second column gives the calculated maximum lengths required for packing each molecule into a space in the crystal. The molecule is assumed to have the normal form of aliphatic chain. Each carbon–carbon bond of length 1·54 Å is projected on a line passing through alternate carbon atoms and the projected length 1·256 Å is taken as the contribution to

[4] Baker, Gilbert, and Ollis, *J.*, 1952, 1443.
[5] Newman and Powell, *J.*, 1952, 3747.

the total distance between the centres of the terminal atoms. The method is extended to other molecules in the later Tables. Distances C–Cl = 1·76, C–Br = 1·91, C–I = 2·10, C–O = 1·43 and O–H = 0·96 Å are projected similarly; the C—O—C angle in ethers is taken as the tetrahedral; in diethylmercury the two C–Hg bonds are assumed to be collinear and of length 2·0 Å. In this way a projected length between terminal atom centres is derived. Normally hydrogen atoms are ignored but in the case of *n*-alcohols the projection of the O–H distance is included. To find the maximum packing length allowance is made for end-groups. For alkanes and halogen derivatives the van der Waals radii Cl = 1·80, Br = 1·95, I = 2·15 or CH_3 = 2·0 Å, are added to the projected lengths between terminal atom centres. For the alcohols a van der Waals radius of 1·2 Å is used for the hydroxyl-H atoms.

Structural Type of Adduct and Dimensions of Included Molecule.—Inclusion compounds of urea or β-quinol are not formed by molecules which have some dimension incompatible with the space available. With tri-*o*-thymotide similar critical dimensions are found but molecules are not divided by these limits into those which do and those which do not form molecular compounds; rather, the dimensions determine which of several structurally different types of molecular compound is formed. This communication excludes wide molecules so that here the length only is involved. As Table 1(A) shows, *n*-alcohols of length less than about 9·5 Å give the cavity-type adduct of simple and fixed molecular ratio $2C_{33}H_{36}O_6$,R·OH. Those of length greater than this form a series of channel-type adducts in which the molecular ratio, although definite for a given alcohol, may not be simple and varies from one to another.

The existence of one type of adduct with very long molecules is evidence for a structure containing extended channels. The compositions confirm this. The longer the chain included in the channel the greater the number of tri-*o*-thymotide molecules required to enclose it. Accordingly, in the Table where figures refer to channel-type unit cells of fixed tri-*o*-thymotide content, the number of included molecules diminishes as the molecular length increases. All molecules listed in Table 1(A) as included in the channel type have similar cross-sections but vary in length. That they fit in the channels without difficulty is apparent from the inclusion (Table 2) of branched molecules without marked changes in cell dimensions. Variation in length of the included molecule has only small effects on the width of the channel or the repeat distance along its structure. To a first approximation the enclosing structure is constant for all adducts of the longer *n*-alcohols. The minor variations, less than 0·2 Å, are considered below. *X*-Ray evidence shows that the channels are parallel to the *c*-axis.

For the other type of adduct a critical length which cannot be exceeded by the included molecule suggests cavities of limited dimensions. As the size of included molecule varies there is, with one exception, no change from the ideal molecular ratio resulting from every cavity's being occupied by a single molecule. Variations up to nearly 1·0 Å in cell dimensions show that in this type the enclosing structure adapts itself to a greater extent to the dimensions of the enclosed molecule, even for the different *n*-alcohols. In β-quinol clathrates hydrogen bonds link the component molecules of the enclosing structure and the cavity can be altered to fit the shape of included molecule only by a process analogous to the stretching of a trellis. Distances between joints remain constant but the shape of the hole alters by increase in one diagonal and decrease in the other. The cell dimensions for pure β-quinol with all its cavities empty are the same as those for the clathrate if the enclosed molecule is small. They are determined by contacts between atoms of the quinol structure itself. A small molecule which is a little too long in one direction to be included in this structure will form a clathrate but, in so doing, causes *c* to increase and *a* to diminish by the trellis extension effect. The behaviour in tri-*o*-thymotide cavity-type adducts is different. Enlargement of the hole can take place in all directions. The available space cannot be completely filled in the methanol compound which has nearly the same cell dimensions as its ethanol analogue. This is confirmed by the observation of

XUM

TABLE 2. *Adducts of tri-o-thymotide with branched molecules.*

Included molecule (A) CORR′ R	R′	Calc. length of included molecule in extended form (Å)	Temp.	Dimensions of unit cell (Å) *a*	*c*	Structure type	Apparent space group	Density (g./c.c. at 20°)	No. of included molecules per unit cell containing 6 tri-*o*-thymotide molecules. † Calc. from cell dimensions and density
CH_3	CH_3	6·5	20°	13·470 ± 0·008	30·273 ± 0·010	Cavity	$P3_121$	1·1689 ± 0·0003	3·06 ± 0·12
C_2H_5	C_2H_5	9·0	19	13·650 ± 0·003	31·064 ± 0·003	,,	,,	1·1359 ± 0·0007	3·00 ± 0·05
A tetraketone *		49·2	—	14·337 ± 0·003	28·958 ± 0·005	Channel	$P6_1$	—	—
(B) R·CO_2R′ R	R′								
H	n-C_3H_7	9·5	—	13·55 ± 0·05	30·5 ± 0·3	Cavity	$P3_121$	1·157 ± 0·001	—
n-$C_{13}H_{25}$	CH_3	20·2	—	14·273 ± 0·001	29·093 ± 0·005	Channel	$P6_1$	1·1293 ± 0·0008	—
(C) CH_2·CHRX R	X								
C_2H_5	Br	8·0	—	13·63 ± 0·05	30·45 ± 0·1	Cavity	$P3_121$	1·1945 ± 0·0007	—
C_6H_{13}	OH	11·9	—	14·24 ± 0·1	29·09 ± 0·1	Channel	$P6_1$	—	—
C_6H_{13}	Br (A)	13·0	—	14·2 ± 0·2	29·1 ± 0·2	,,	,,	1·193 ± 0·0007	—
C_6H_{13}	Br (B)	13·0	—	14·426 ± 0·003	28·911 ± 0·003	,,	,,	—	—

* CH_3·$[CH_2]_7$·CO·CH_2·CO·$[CH_2]_7$·CO·CH_2·CO·$[CH_2]_7$·CH_3. † Given only when the constants are all known with sufficient accuracy.

TABLE 3. *Some diffraction effects due to molecules included in the channel structure.*

Included molecule	Approx. length calc. for molecule in extended form (Å)	Spacing calc. from one-dimensional layer streaks (Å)	Assumed orders of observed streaks (*c*-axis oscillation)	No. of included molecules per unit cell Ideal, calc. from spacing of third column	Calc. from unit cell weight
n-Butyl iodide	9·6	—	None obs.	—	—
n-Pentyl bromide (A)	10·5	8·8	1, 2	3·3	—
,, (B)	10·5	9·6	† 1, 2	3·0	3·02 ± 0·03
n-Pentyl iodide	10·9	—	None obs.	—	—
n-Hexyl bromide	11·7	11	2	2·6	2·74 ± 0·12
n-Heptyl bromide	13·1	12	3	2·4	2·40 ± 0·04
n-Heptyl iodide	13·4	12·5	2, 3	2·3	2·40 ± 0·02
n-Octyl bromide	14·3	13·5	2, 3	2·1	2·14 ± 0·04
n-Octyl iodide (A)	14·7	14·5	* 2, 4	2·0	1·95 ± 0·02
,, (B)	14·7	—	§ None obs.	—	—
n-Hexadecyl bromide	24·4	24	3, 4, 5, 6, 7	1·2	1·36 ± 0·02
n-Hexadecyl iodide	24·7	24	4, 6, 7	1·2	0·95 ± 0·04
n-Octadecyl bromide	26·9	26	1, 2, 3, 4, 5	1·1	1·26 ± 0·01
n-Octadecyl iodide (A)	27·2	27	2, 3, 4, 5, 6, 7, 8	1·1	1·19 ± 0·01
,, (B)	27·2	—	None obs.	—	—
2-Bromo-octane	13·1	12 × 2	‖ 1, 2, 3, 4, 6	2·4	2·49 ± 0·02
Hexamethylene di-iodide	14·0	12·5	‡ 1, 2, 3	2·3	—
Diethyl mercury	9·8	9·7	† 1, 3	3·0	—
Methoxybutane	10·1	9·7	† 1	3·0	3·03 ± 0·05
Ethoxybutane	11·4	9·7	† 1	3·0	3·03 ± 0·04

(A) (B) indicate that two crystalline forms are found. * Coincident with 4th and 8th sharp layers. † Coincident with 3rd, 3rd and 6th, or 3rd and 9th sharp layers. ‡ Also streaks corresponding to 3·5 Å. § Additional sharp spots on 4th and 8th layers. ‖ Molecules presumed paired, head-to-head.

approximately the same values for crystals of tri-*o*-thymotide which have been obtained in a trigonal form with most of the cavities unoccupied. As the length of the included molecule increases beyond that of ethanol the cavity is steadily enlarged. Both *a* and *c* increase; there is no factor analogous to the hydrogen bonding of quinol to link an increase in one with a diminution in the other. The enclosing molecules merely move further apart. Although the length of the included molecule is varied considerably the unit-cell dimensions do not change by more than 1·0 Å between the smallest and the largest member of the series. Evidently there is in the unexpanded structure a space nearly sufficient to hold the largest of the molecules shown as giving the cavity-type adduct. To accommodate a molecule lengthened by a further CH_2 group would require a relatively big increase of about 1·5 Å in at least one lattice dimension which might, by creating space other than that needed for the larger molecule itself, lead to instability. Lengthening the molecule beyond a certain limit in fact results in formation of the channel structure.

The methanol adduct appears anomalous. The cell dimensions given in Table 1 are slightly greater than those of the ethanol analogue. Sometimes methanol solutions deposit unsolvated tri-*o*-thymotide and occasionally a different adduct of monoclinic form has been obtained. Attempts to prepare the trigonal cavity-type adduct by crystallisation of the pure unsolvated tri-*o*-thymotide from pure methanol failed. The adduct could be obtained from ordinary laboratory methanol on seeding with a little of the acetone adduct and the cell dimensions given are derived from a crystal of this origin. It is thought that a little acetone or other impurity must be included. This will account for cell dimensions larger than those expected. In view of this circumstance an accurate determination of molecular ratio is impossible for this adduct, and no density is recorded.

The critical limit of length is estimated from the behaviour of *n*-pentyl alcohol. In some crystallisations this acts as a short molecule forming a cavity-type adduct which, however, has cell dimensions close to the largest observed in the series. When left in the mother-liquor at room temperature these crystals change into the orthorhombic form of pure tri-*o*-thymotide. In other crystallisations the solution deposits crystals of the channel-type appropriate to a long-molecule adduct. It appears therefore that the greatest length of the *n*-pentyl alcohol molecule is very close to the critical limit for a short molecule.

The existence of this limit has been confirmed by examination of adducts with molecules other than *n*-alcohols. In Table 1, parts B—F give constants for other unbranched molecules. The included molecules of Table 2 have a single atom or methyl group branching from the main chain. Alkyl halides, polymethylene dihalides, esters, ketones, and ethers are found among the molecules of length not greater than 9·5 Å, which form cavity-type adducts. Channel-type adducts have been made with molecules of all these types with lengths greater than 9·5 Å. That *n*-pentyl bromide behaves as a long molecule agrees with the conclusion that *n*-pentyl alcohol, slightly smaller, is just on the limit.

The unit-cell dimensions for both the cavity- and the channel-type adducts formed by this variety of molecule have, within a few hundredths of an Ångström unit, the same limits of variation as the corresponding *n*-alcohol adducts. Even if it contains one of the branched molecules of Table 2, the channel-type varies much less than the cavity-type containing unbranched molecules.

Space requirements alone do not exclude short molecules from the channel type, but no very short molecule has been found to enter this structure. For molecules with greatest dimension near the limit, behaviour varies and seems to indicate difficulty in formation of the cavity structure. In one instance, that of *n*-pentane, the only adduct found is of channel type although the cavity form is expected. Sometimes one or more crystalline forms can be obtained in addition to the cavity-type adduct. These may, but do not always, include a channel form. Thus *n*-butyl bromide gives the cavity form only, whereas from solutions of tri-*o*-thymotide in *n*-butyl iodide three different adducts have been obtained, cavity and channel forms, and a third type which has not been examined

Methoxybutane	10·1	9·7	†	3·0	3·03 ± 0·05
Ethoxybutane	11·4	9·7	†	3·0	3·03 ± 0·04

(A) (B) indicate that two crystalline forms are found. * Coincident with 4th and 8th sharp layers. † Coincident with 3rd, 3rd and 6th, or 3rd and 9th sharp layers. ‡ Also streaks corresponding to 3·6 Å. § Additional sharp spots on 4th and 8th layers. || Molecules presumed paired, head-to-head.

XUM

in detail. Trimethylene dibromide gives as a second form an orthorhombic compound $2C_{33}H_{36}O_6,Br\cdot[CH_2]_3\cdot Br$ of a type so far found with this molecule only. Some diethyl ether solutions deposit orthorhombic crystals of an adduct. These rapidly lose ether on exposure to air, and are metastable with respect to the cavity-type.

In urea adducts the enclosed molecule must have a minimum length in order that the van der Waals interaction shall be sufficient to retain it. As may be expected the minimum is not a fixed length but depends on the nature of the included molecule. Thus acetone, butyric acid, and hexan-1-ol, although of different lengths, are the shortest molecules of their homologous series which form urea adducts.[2] For the tri-*o*-thymotide channel adducts any consideration of a lower length limit must take into account the possibility of the alternative cavity structure. If a molecule below the upper limit of size for the cavity type does not form a channel adduct, it may be for reasons analogous to those applicable in the urea adducts, or simply that the cavity-type adduct is more stable. Whichever explanation holds, a lower limit of length required for formation of the channel type is not fixed geometrically like the upper limit for the cavity type, and if it existed, would not necessarily have the same value as this upper limit.

The relative stabilities of the three tri-*o*-thymotide structures may be roughly compared by means of the closeness of molecular packing. Approximate values for the space in the crystal per molecule of tri-*o*-thymotide present, are 750 Å^3 in the racemic unsolvated form, 790 Å^3 in the cavity-type unsolvated crystal, and 851 Å^3 in the most closely packed channel structure. The channel type does not appear to be formed without included molecules. Presumably it is too open. The cavity type, so far as the tri-*o*-thymotide molecules are concerned, is more densely packed and is usually formed in preference to the channel type unless the length of included molecule forbids. It may be obtained with nearly all cavities empty but this form is metastable with respect to the still more closely packed orthorhombic unsolvated form.

Symmetry and Molecular Arrangement in Channel-type Adducts.—Results recorded in Tables 1 and 2 have led to general conclusions concerning the crystal structures of the two types of adduct, in particular the nature of the spaces available for the included molecule. These conclusions do not require or imply detailed information about the atomic arrangements. The rule concerning maximum length of included molecule in the cavity type can be applied empirically, but any structural details obtainable should help to explain it. Those given below concern the positions of molecules and spaces rather than of individual atoms. A complete determination of atomic parameters, although feasible, would be very lengthy owing to the general complexity of the structures, and the large number of parameters. A favourable circumstance is the occurrence of so many related structures and freedom to substitute heavy atoms for phase determination. Against this, however, must be set the combination of a three-fold or six-fold screw axis with non-centrosymmetry. As will appear also, heavy atoms introduced in the included molecules do not necessarily go into the structure in an ordered manner, and thus may complicate rather than simplify the phase problem.

Channel-type structures will be considered first. The unit cells of those with space group $P6_1$ (or $P6_5$) always have considerably less than six included molecules although there is no position of less than six-fold multiplicity in this space-group. There is evidence that the packing of tri-*o*-thymotide molecules leaves an array of channels parallel to the *c* axis and that in these the other molecules are enclosed in their extended chain forms with greatest lengths parallel to the channels. The conformity of some of the structures as a whole with space-group symmetry $P6_1$ may therefore be illusory. From their dimensions alone it follows that many of the included molecules must occupy positions in the unit cell which do not have a constant parameter at least along the *c* axis. Consequent disorder effects mentioned below as more readily detectable when the included molecule contains a heavy atom may, in the absence of a heavy atom, usually be so weak as to escape observation. It is convenient therefore to consider first the arrangement of the tri-*o*-thymotide

molecules alone, and to use space-group terms which strictly do not apply to a disordered structure as a whole.

For the channel-type adducts with *n*-alcohols and *n*-alkyl halides the unit-cell dimensions, which vary little with included substance, indicate an unchanging assembly of tri-*o*-thymotide molecules. This is confirmed by the intensities of the *X*-ray reflections. Provided the included molecules contain no heavy atoms, little change is observed in the intensities of $0kil$ reflections when one molecule is substituted for another. A large number of atoms of the structure as a whole must therefore remain in the same position. This would be the case if the six tri-*o*-thymotide molecules preserved a constant arrangement in accordance with $P6_1$ (or $P6_5$) on a six-fold spiral. Pure tri-*o*-thymotide has not been obtained directly in the channel form but a partial indirect realisation supports the view that this six-fold spiral is the arrangement in all structures of this type. For the adduct with diethylmercury, approximate molecular length $= c/3$, the absent spectra $000l$ when $l \neq 3n$ and the intensity relations indicate space-group $P6_2$ (or enantiomorphous $P6_4$). Under the influence of *X*-rays, or more slowly without, the crystals darken through decomposition of the diethylmercury. Simultaneously the weak reflections $000l$ where $l = 3$, 9, or 15 disappear. The space-group then appears to be $P6_1$. The crystal still gives the characteristic single crystal pattern of sharp *X*-ray reflections though there is some breaking up of spots in the high orders and powder lines of decomposition products are superposed. This shows that the tri-*o*-thymotide spiral alone results in the absence of $000l$ for $l \neq 6n$. Included diethylmercury molecules repeat at intervals of $c/3$ with or without relative rotation about this axis. The two components of the combined structure have in common the condition for the absence of $000l$ where $l \neq 3n$. Complete or partial decomposition of included molecules destroys the regularity which produces thirding. Evidently such decomposition can take place to an appreciable degree without collapse of the enclosing structure. The channel adducts formally belonging to $P3_1$ (or $P3_2$) significantly contain only molecules which, having extended lengths fairly close to $c/3$, could give similar thirded structures. The few adducts which formally belong to $P6_2$ must therefore have a structure very similar to those in $P6_1$. As mentioned, the *n*-hexane adduct ($P3_1$) gives a diffraction pattern which differs very little from that expected for $P6_2$ to which it was at first supposed to belong. If the structure in fact has a symmetry $P6_2$ the 6_1 spiral would have to be modified by displacement of molecules parallel to *c*. In view of the closeness of cell dimensions and similarities in the intensities of *X*-ray reflections, such a change seems unlikely and those crystals which appear to have space-group $P6_2$ or $P3_1$ are therefore considered to have the 6_1 spiral. It may be that differences in intensities of $hkil$ and $hki\bar{l}$ reflections are too small for observation or are obscured by twinning on (0001).

In the space-group $P6_1$ the six tri-*o*-thymotide molecules must lie in general positions forming a six-fold spiral. There are no special positions. The exact form of the tri-*o*-thymotide molecule is not known. It is not planar but is folded so that there is no significant empty space in the middle of the central twelve-membered ring. This conclusion is based on the construction of scale models which show that it has roughly the form of a discus, somewhat distorted from the circular and with protuberances, particularly due to the three *iso*propyl groups. That the molecule may not have the three-fold axis suggested by the formula appears from the infrared absorption spectra of orthorhombic unsolvated tri-*o*-thymotide and of the acetone adduct. Examined in the form of Nujol mulls both give evidence that one of the three carbonyl groups of the tri-*o*-thymotide molecule differs from the other two. The spectra of the two materials can be distinguished only by effects due to the carbonyl group of the acetone. Packing considerations show that the tri-*o*-thymotide molecules can be arranged with the flat of the discus approximately parallel to the spiral axis, but not perpendicular to it.

The structure therefore consists of tri-*o*-thymotide molecules spirally arranged around channels parallel to the *c* axis (Fig. 1). The other molecules are enclosed, in their extended

XUM

chain forms, with their greatest lengths parallel to the channels. The packing lengths of the extended forms of the molecules of hexadecyl bromide, 24 Å, and octadecyl alcohol, 26 Å, are considerably greater than the *a* dimension, 14·3 Å, of the unit cell. For a completely ordered structure it could be concluded that these molecules must have their lengths far from parallel to *a*, but when channels are postulated the argument is inapplicable. The tetraketone included in Table 2 has a molecular length of 49 Å. To contain such a molecule, longer than any line across a single unit cell, the channels must continue into adjacent cells and therefore extend throughout the whole crystal. Cell dimensions provide evidence for the direction of the channels only when branched molecules are considered. For the adduct formed by 2-bromo-octane, *a* is greater by 0·1 Å, and *c* is less by 0·12 Å than the corresponding dimensions for the *n*-heptyl bromide adduct. To accommodate the greater width of the molecules the channels must have opened out, and they are thus shown to be parallel to the *c* axis. This spreading out of the tri-*o*-thymotide molecules incidentally makes possible a unit-cell contraction in the *c* direction.

Since the branched molecule requires only a slight increase in channel cross-section there must be more than enough space for the straight-chain molecules. This would allow them to have various orientations in the channels and so to preserve the apparent 6-fold symmetry.

Although the space-group symmetry is $P6_1$ the number of channels per unit cell is not necessarily a multiple of six. The extension of the channels parallel to *c* reduces the symmetry problem to that of the corresponding plane group P6. In this the general position remains 6-fold but there are special positions of 3-fold, 2-fold, and 1-fold multiplicity. There is strong evidence for a single channel per unit cell.

For some adducts such as that of *n*-pentyl iodide there are three molecules, each of length approximately *c*/3, per unit cell. If the molecules were in separate channels a greater number could be included. As soon as the included molecule has more than one-third of the length of the *c* axis, less than three molecules are included per unit cell. They must therefore be placed one on top of the other in a single channel centred on the origin.

X-Ray Diffraction due to Material included in the Channels.—Direct *X*-ray evidence supports the channel structure. Diffraction patterns obtained from crystals oscillating about the symmetry axis in certain instances show more or less continuous streaks parallel to the layer lines of sharp reflections that correspond to the unit cell. Such effects which have been observed with other crystals [6] are due to diffraction by a part of the structure which behaves as a one-dimensional diffraction grating for *X*-rays. Even on long exposures they are usually not observable for the tri-*o*-thymotide adducts unless the included molecule contains a heavy atom. A one-dimensional grating gives its layer-line diffraction effect without the oscillation needed for a three-dimensional crystal grating. The Plate shows a diffraction pattern obtained with a stationary crystal of the 2-bromo-octane adduct. Copper radiation filtered through nickel foil was used. The *c*-axis was vertical but, without oscillation, only a few of the sharp reflections on the normal layer-lines have appeared. For these few the corresponding planes happened to be in the reflecting positions for the characteristic radiation. Continuous horizontal lines also due to diffraction of the K_α radiation may be seen without the confusion of ordinary layer-lines, together with other diffraction effects, chiefly a Laue pattern formed by diffraction of the white component of the imperfectly filtered radiation. A number of diffuse reflections may be seen on vertical row-lines. They correspond in position to Bragg reflections. The crystal was, however, not in a position to give the Bragg reflections and the diffuse spots observed are due to imperfections, either static or dynamic, of the lattice.

Table 3 records streaks parallel to the layer lines observed in diffraction patterns obtained by the normal technique with single crystals oscillating about the *c* axis. For the different members of the series of channel adducts, the intermediate streaks vary in

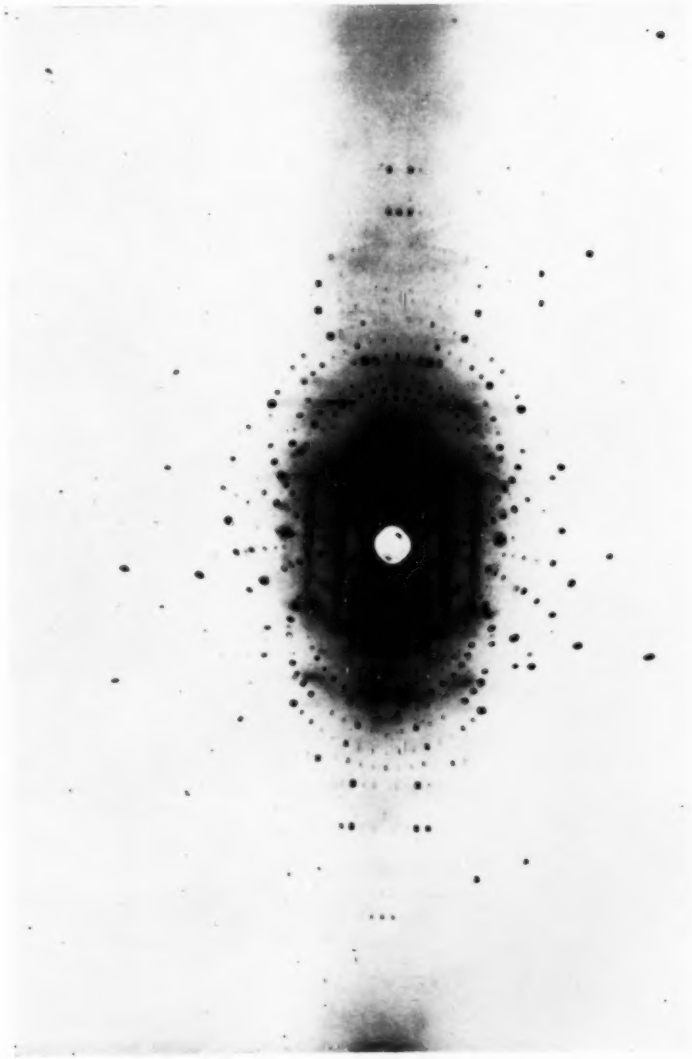
[6] Borchert and Dietrich, *Heidelberger Beitr. Mineral.*, 1952, **3**, 124.

XUM

XUM

XUM

X-*Ray diffraction pattern given by stationary crystal of 2-bromo-octane adduct. The axis of the cylindrical film, to which the c-axis of the crystal was parallel, is here horizontal.*



[*To face p.* 2348.

FIG. 1. *Schematic representation of spiral arrangement of molecules forming the channels. Each molecule denoted by a line; the nearby figures indicate relative displacements of molecules in fractions of c axis length. Vertical screw axes are indicated by* 6_1, 3_1, *and* 2_1.

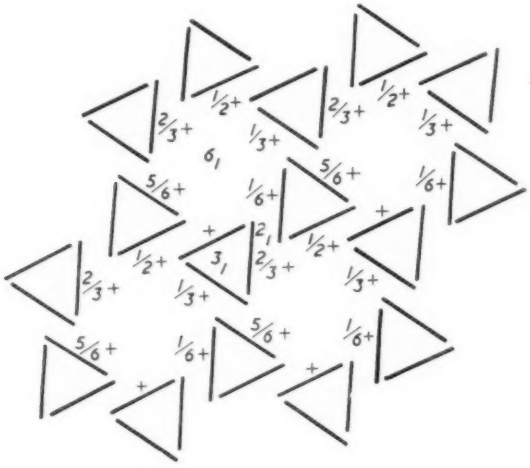
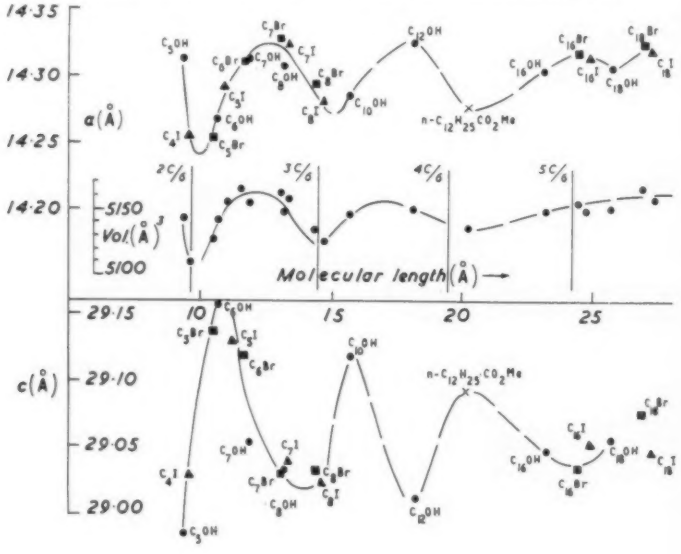


FIG. 2. *Variation of cell dimensions and volume with length of included molecule in channel. In the plots of a and c, alcohols shown by circles, bromides as squares, and iodides as triangles.*



XUM

position according to the length of the included molecule, being related to its repeat distance in the channel. There is no relation other than accidental between this distance and the *c* dimension of the unit cell. Certain included molecules have a packing length which is a simple fraction of *c*. In such a case there is a common unit translational repeat distance parallel to *c* and these adducts either do not show streaks or have them coincident with the layer-lines of sharp spots.

For the hexamethylene di-iodide adduct three streaks are observed which correspond to the first three layer-lines of a structure with repeat distance 12·5 Å. This is very close to the expected packing length of hexamethylene di-iodide and may therefore be taken as the repeat distance of the molecules included in the channels. The smallest *c* dimension divisible by both 29 and 12·5 Å (approximately) is 87 Å. For a pattern of this repeat distance the observed streaks would be the 7th, 14th, and 21st layer-lines. A fourth and rather sharp streak corresponds to a spacing of 3·5 Å and may be indexed as the 25th layer for the 87 Å spacing. The first three observed layers are strong because they correspond to the repeat distance 12·5 Å between similar iodine atoms of successive molecules. The fourth streak is sharp and prominent because the 3·5 Å spacing corresponds to the distance parallel to *c* between the iodine at the end of one molecule and its near neighbour, an iodine of the next molecule. On the basis of the included molecule length 12·5 Å this streak has to be assigned a fractional order $3\frac{4}{7}$ or about $3\frac{1}{2}$. For the other included molecules simple orders may be readily assigned to the observed layer streaks and consistent one-dimensional lattice spacings calculated. In Table 3 the lengths of a series of alkyl halides and a few other molecules are compared with the calculated spacings. Some of the streaks are difficult to observe accurately and the agreement is considered good for most of the long molecules. The change in spacing for each $-CH_2-$ group is approximately as expected. The maximum length has been calculated in all cases and generally this is slightly larger than the observed spacing. Any difference may be explained by the way in which the end-groups fit together. The spacing calculated for the *n*-pentyl bromide adduct is, however, considerably less than the packing length. For such short molecules the calculated length is likely to differ from the repeat distance. Since the channels are broader than is necessary to hold the *n*-halides, a short chain, the axis of which has been assumed parallel to the *c*-axis for purpose of calculating the repeat length, may in fact be inclined to *c*. A comparison of the *n*-pentyl bromide and the *n*-hexyl bromide streaks shows an increase in the packing length of 2·4 Å as a result of the addition of a single CH_2 group. With all allowance for experimental inaccuracy, this is far beyond the projected length 1·256 Å or even the maximum 1·54 Å which could occur if an extra C–C bond had been added, without any other change, to the atoms as they are placed in the *n*-pentyl bromide adduct. The over-all lengths of the higher members of the series evidently require them to be nearly parallel to *c*. Successive removal of many CH_2 groups may permit only a small variation in inclination of molecular length to the channel axis but, at some stage, one such removal may result in a very large change in inclination. An extreme case would be that of *n*-alkanes in a channel of such width that ethane could just lie broadside on. Evidently the large change occurs because *n*-pentyl bromide is short enough to be noticeably tilted across the channel whereas *n*-hexyl bromide is nearly parallel to it. An even greater change of inclination would be expected if *n*-butyl bromide could be substituted for *n*-pentyl bromide. With this may be connected the change to cavity type which occurs when the attempt is made.

Ideal Compositions of Channel-type Adducts.—The one-dimensional layer line spacing may be used to calculate what may be called an ideal composition of the adduct. Divided into the corresponding value of the *c*-dimension given in Table 1 or 2, it should give a maximum number of molecules that can be fitted into the single channel of the unit cell containing six tri-*o*-thymotide molecules. The resulting figures are compared in Table 3 with the number of included molecules estimated from the unit cell weight. The general agreement shows that in most cases the channels are filled. A value from cell weight

XUM

lower than the " ideal " could be explained by unoccupied spaces in the channels. The " ideal " value should never be the lower of the two by an amount exceeding possible errors of measurement, which are mainly in the " ideal " compositions derived from faint and diffuse streaks and may amount to a few per cent. The Table shows that his requirement is satisfied except possibly for the hexadecyl bromide and the octadecyl bromide adduct.

The channel-type adducts as a group are distinguished from those of the cavity type in having an ideal ratio of included molecule to tri-*o*-thymotide which varies with molecular length. For each adduct the ratio of molecules is in practice definite although it may not be simple. However, even if any departures from ideal molecular ratios are ignored, the two types cannot be contrasted as stoicheiometric and non-stoicheiometric, since some of the channel adducts have rational compositions. As far as the compositions alone are concerned it is more appropriate, in this type of molecular compound, to distinguish rational and irrational. Non-stoicheiometry implies disorder, and varying displacement of included molecules relative to a fixed part of the channel is the form of disorder here associated with an irrational composition. However, varying displacements in different channels are possible when the molecular length accidentally requires a simple ratio, so that this simple ratio does not seem in principle different from any other relation. The channels diminish in length with increase of temperature but the effective lengths of enclosed molecules will increase. Structurally it would therefore be possible for the ratio to vary slightly with the temperature of preparation. The effect is beyond the limits of the present measurements, but the possibility makes the description " stoicheiometric " unsuitable.

Order and Disorder in the Channels.—The *X*-ray diffraction effects show at least two kinds of channel adduct according to the degree of order. Constant spacing of the included molecules in the channel gives rise to a one-dimensional grating effect if the structure is disordered in certain other ways. Where the length of included molecule requires displacements along the channel it seems unlikely that the molecules in one channel could restrict the positions of those in any other. The individual one-dimensional gratings are kept parallel and equally spaced by the channels but their molecules do not form a three-dimensional lattice. This will account for the observed streaks. When the length of included molecule is rationally related to the *c* dimension a more regular arrangement could occur, each included molecule being displaced a similar distance along the channel relative to an origin of the unit cell. Since the channels have a six-fold spiral structure such regularity might be expected when the length of included molecule is a multiple of $c/6$, *i.e.* $n \times 4{\cdot}84$ Å. The case of $n = 1$ does not arise because such a short molecule will form a cavity-type adduct, but the list of included molecules contains several examples where the molecular length is approximately a higher multiple of 4·84 Å. The small variations of the nearly constant unit-cell dimensions provide evidence for the more regular arrangement. Plotted in Fig. 2 they show a periodic variation of both *a* and *c* with length of included molecule. As *c* increases, *a* diminishes, so that roughly the top and bottom curves of Fig. 2 are mirror images in a plane between then. The minima in *c*, and the corresponding maxima in *a*, are separated from each other at intervals which are near to multiples of 4·84 Å along the molecular length axis. Also they occur at molecular lengths which are themselves not very different from $n \times 4{\cdot}84$ Å where n is 2, 3, 4, or 5. For consistency, the maximum molecular lengths, as calculated above from atomic dimensions, have been used in the graph. As has been shown, these, especially for the shorter molecules, are rather larger than the effective lengths and the points as plotted should perhaps be displaced by an uncertain and variable amount, never likely to be much more than 1 Å, to the left. This brings most of the minima in *a* and the maxima in *c* closer to positions at $n \times c/6$ on the horizontal axis.

These unit-cell dimensions are determined by the way in which the component molecules fit together. Regular repetition of included molecules, always with similar

surroundings, may result in a slightly different, and, it would be expected, closer packing of the tri-*o*-thymotide components than is attainable when arbitrary displacements of included molecules along the channels must be allowed.

The middle curve of Fig. 2 shows the volumes of the unit cell plotted against the same scale of molecular lengths. The overall result of the opposed changes in a and c is to produce minima in the cell volume for lengths of included molecule which are close to $n \times c/6$. All the curves of Fig. 2 have to be drawn from relatively few points except in the region 9—16 Å. The positions of the maxima in c do not exactly coincide with those of minima in a, or either of these with the minima in volume. Even if there were no difficulty in tracing the curves or uncertainty in the absolute scale for molecular length, there would be no reason why they should. In the absence of finer structural detail which might explain everything, the idea that an improved packing of the structure takes place for molecules of lengths which are multiples of the spiral component $c/6$ is based on the periodicity common to all three curves and the occurrence of minima in a and in the volume at molecular lengths somewhere near to $n \times 4{\cdot}84$ Å, rather than on any exact coincidence. A slightly closer fit of the molecules forming the channel may be imagined. This may be illustrated by a set of ball-ended rods enclosed between extended corrugated sheets. As the length of rod, imagined to lie across the corrugations, steadily increases, the separation between the sheets will vary periodically, with minima when all the ball-ends lie in hollows. Any such manner of packing included material so that its protuberances have the same periodicity as the indentations of its surroundings, should lead to similar effects.

The increase in a produced by inclusion of a branched molecule may be greater than the periodic variations. Points plotted in Fig. 2 therefore refer to unbranched molecules. The sole exception is methyl laurate which may be considered only slightly branched. The values, included because others were not available in that region, fit well with the general trend of the curves.

Since, when close fitting occurs, a decreases, the tri-*o*-thymotide molecules are drawn together in two dimensions and the spaces between them are diminished. The increase in c is regarded as consequential, the tri-*o*-thymotide neighbours projecting into these spaces from the direction of the third dimension being forced outwards. For the shortest molecules, of length about 10 Å, the cell volume varies by about 1% between the closest and loosest packing. As the length of molecule increases there will be a smaller proportion of places in the channel where the ends make a closer fit. The oscillations in the curves for cell dimensions and cell volume therefore diminish in amplitude, tending on the right towards limiting values appropriate to an indefinitely extended polymethylene chain. The volumes seem to approach a limit which is not less than any value for a shorter molecule. Similarly the limiting value for a is about equal to the maximum values reached in the intermediate positions where the included molecules do not make their closest fitting, *i.e.*, as the proportion of close-fitting places becomes less the minimum in a rises, but the maximum is unchanged. This behaviour is consistent with the idea that widening of the channels is the primary effect. The consequential change does not require the limiting value of c to be the same as the lowest of its minima.

Between molecular lengths of $9\frac{1}{2}$ and 15 Å the curves of Fig. 2 can be traced without use of the results for alcohols. The values for the alcohols fit the curve well in this region and this suggests that the molecular lengths used are approximately correct, and that the channels contain single molecules. If they contained hydrogen-bonded double molecules, the points plotted in the Figure for alcohols would have to be displaced to positions somewhat less than double the molecular length shown. It may be seen that such changes would destroy the regularities which the forms of the curves strongly suggest are based on a structural reality.

When displacements along the channel are constant other structural regularities are possible. If all the included molecules also have orientations which are either the same or related by the 6_1 screw axis the structure as a whole forms a three-dimensional lattice

XUM

which will give no one-dimensional layer-line streaks. When the orientations are unrelated to each other or are related but irregular in sequence the structure is disordered even though the length of included molecule is commensurable with the channel c spacing. Irregularities could be connected with the sequence in any one channel or with the relation between one channel or region of the crystal and others. These disordered structures should give various diffraction effects including layer-line streaks. Among adducts formed by molecules of these special lengths there appear to be examples of both ordered and disordered forms.

The *n*-pentyl bromide adduct has three included molecules, of effective length about $c/3$, per unit cell. Only the faintest layer-line streaks have been observed, some heavily exposed oscillation photographs showing no signs of disorder. For one specimen the streaks give the expected $c/3$ (9·6 Å) spacing in the channels but for another the spacing is different (8·8 Å). Two explanations are possible for the faintness of streaks. There may be only a few disordered molecules or the disorientation may be obscured because the bromine atoms contribute only to the sharp normal reflexions. Being a terminal substituent and fairly large, each bromine may fit the channel in the same way and provide an anchor so that only the rest of the molecule can vary in its orientation. In that case the effect of disorder among the lighter atoms would be no stronger than for the *n*-alcohol series where, in practice, it cannot be observed. It is less likely that such anchors can be placed in line parallel to c when they have varying displacements relative to their surroundings, and in this case the halogen atoms will contribute to the disorder streaks. The adduct of *n*-butyl iodide with a unit-cell volume very close to the first minimum in Fig. 2 gives no streaks. Probably the effective length of the molecule is a little less than $c/3$. The general behaviour that molecules are packed as closely as possible in the channels according to their length may break down when the included molecule has a length very nearly equal to $c/3$. On this view, which is supported by the compositions, the *n*-butyl iodide molecules leave some channel space unoccupied, and thus achieve a periodicity simply related to that of the surroundings. The *n*-pentyl iodide adduct also gives no layer-line streaks, although the effective molecular length is expected to be slighty greater than $c/3$. In this case it may be necessary for the molecule to adapt its orientation, conformation, or inclination to the channel length to attain a periodicity commensurable with c. Adaptation of either the slightly longer or slightly shorter molecule to channel periodicity is accompanied by a more complete order of the whole structure. This is shown, not only by the absence of layer-line streaks, but also by the appearance of the sharp reflections $000l$, where $l = 3n$, which cause the formal space-group to be $P3_1$. The second form of *n*-pentyl bromide for which the streaks give a spacing of 8·8 Å indicates that although molecules of approximately the right length may adapt in this way to the channel periodicity, they sometimes behave otherwise.

Two adducts are formed by *n*-octyl iodide which has a molecular length approximately $c/2$. One (B) shows no disorder effects and the other (A) has streaks coincident with the 4th and the 8th c layer-lines. To reconcile the positions of the streaks with the molecular length it is necesary to take them as the 2nd and the 4th order. The extinction of odd-order layers may be attributed to the presence of channels containing molecules in certain positions and an equal number of channels with molecules similarly placed except for a relative displacement of half the molecular length, *i.e.*, $\pm c/4$ Form (B) shows the complication that additional sharp reflexions, occurring instead of streaks on the 4th and the 8th c layers, can be indexed on the basis of a hexagonal cell of seven times the normal a-dimension. That extra reflexions are unobserved for all except the $4n$th layers may be attributed in this form also to the presence of included molecules in two or more positions with relative displacements of $c/4$. If there is no disorder these must be in different channels and, strictly, an even number of filled channels is required for complete interference to be possible when $l \neq 4n$. The unit cell has 49 channels and the effect of the odd one might be slight among so many. It is possible, however, to devise structures

consistent with the space-group in which $(6n + 1)$ channels ($n = 0,1,2\ldots$) are unoccupied. They have an even number of filled channels per unit cell, and some such structure may be necessary to account for the 7-fold enlargement of *a*. Presumably the disordered form (A) has similar filling of channels with *c*/4 relative displacements but lacks regularity of sequence in neighbouring channels. Octadecyl iodide forms a disordered structure (A) with streaks corresponding to a spacing of 27 Å. An ordered form (B) has no streaks and presumably the molecules are adapted so that they repeat regularly at the slightly greater distance 29 Å of the *c* dimension. The lower density of the (B) form is in agreement with there being some empty space. Adducts of diethylmercury, methoxybutane, and ethoxybutane all give streaks coincident with sharp layers. The molecular lengths, 9·8, 10·1, and 11·4 Å respectively, are close to *c*/3 or, in the case of ethoxybutane, must be adapted to it, but there is disorder similar to that in form (A) of the *n*-octyl iodide adduct.

Cavity-type Structures.—In the cavity-type adducts molecules of tri-*o*-thymotide are arranged in trigonal (3_1) spirals, the two spirals passing through a unit cell ($a = 13{\cdot}5$ Å) being related to each other by a two-fold symmetry axis parallel to *a*. The cell dimensions are readily distinguishable from those of the channel adducts in which the molecules may be regarded (Fig. 1) as lying on 3_1 spirals related by a two-fold screw axis parallel to *c*, but are sufficiently similar to them to suggest related arrangement of tri-*o*-thymotide molecules in the two structures. However, the spaces for the included molecules in the cavity-type adducts are not merely smaller forms of the hexagonal channel. They differ in character and position. That they are not continuous channels is shown by the existence of an upper limit of length of included molecule. The volume in the crystals per tri-*o*-thymotide molecule suggests about half as much space available for inclusion as in the channel type. Since in certain cases a small increase in the width of a molecule due to the replacement of one substituent by another results in the cavity-type adduct's not being formed, it is concluded that the cavities are limited crosswise and may be considered as roughly cigar-shaped. The unit cell contains three included molecules which formally could occupy either of the special positions $x0\frac{5}{6}$ or $x0\frac{1}{3}$. Both these require the molecule to have a two-fold symmetry axis. A number of the included molecules have this symmetry but many do not. Some therefore cannot be arranged in accordance with strict space-group symmetry and this limits the validity of any arguments designed to locate the cavities by symmetry considerations. Some evidence is provided by the iodine adduct. Its crystals are pleochroic, transmitting red light when the electric vector is perpendicular to *c* and yellow light when it is parallel. The length of the iodine molecule, and hence, it is assumed, the length of the cavity, is therefore not parallel to *c*. Though not necessarily perpendicular to *c* it is inclined at a considerable angle to it. Structural investigations of the methylene iodide adduct in which the iodine atoms may be located because of their high scattering factor show that the line joining centres of the two iodine atoms lies at right angles to the *a* axis and is inclined at about 16° to a plane parallel to (0001). The over-all contact length for this direction of the molecule is 7·7 Å. This is greater than the permitted width of the molecule and may be expected to lie approximately in the direction of the cigar length.

The cavity-type adducts of the *n*-alcohols are shown in Table 1 as having space-group $P3_121$ with *a* and *c* approximately 13·5 and 30·5 Å respectively. The other adducts of this kind in Tables 1 and 2 have a similar *c*-dimension, but those formed by halogen-substituted alkanes often have the *a*-dimension doubled. In the Tables this is recorded as 13·5 (approx.) × 2. The structure may be ordered, giving sharp reflexions, on the whole weaker than the rest, corresponding to the doubled *a*-dimension, or it may be disordered. For both kinds, as for those without doubled *a*, oscillation photographs show repetition every 120° around the *c*-axis and in general the intensity of *hkil* is not equal to that of $hki\bar{l}$. The only systematic absence is that of $000l$ when $l \neq 3n$. The equality in intensities of reflexions *hki*0 and *khi*0 shown, for example, by the symmetry in oscillation photographs taken around the *a*-axis establishes the presence of the two-fold symmetry

axis. The space-group remains $P3_121$ in spite of the doubling of *a*. The disordered structures do not show sharp spots corresponding to doubling of *a* but give streaks along the direction of a^* in the reciprocal lattice. In the ordered structures presumably the included molecules have alternative orientations in regular sequence along *a*. The streaks could be explained by an irregular sequence. Unit cells with doubled *a* dimension are given by the adducts of *n*-propyl bromide (B), *n*-propyl iodide, *n*-butyl bromide, and trimethylene dibromide (B). Disordered forms are given by *n*-propyl bromide (A), *n*-butyl alcohol, ethylene dichloride, and ethylene dibromide. Of the two forms given by *n*-propyl bromide the more ordered was obtained by slower crystallisation, but it is not known whether this is accidental or not.

Optical Resolution.—Crystallisation of each trigonal or hexagonal compound constitutes a new example of spontaneous optical resolution similar to that already shown experimentally for the *n*-hexane and the benzene adduct. Some of the unit cells contain six molecules of tri-*o*-thymotide, just enough to occupy one set of space-group positions which are equivalent, and the crystal therefore must contain tri-*o*-thymotide molecules of one configuration only. The resolution has been confirmed polarimetrically for adducts with *sec.*-butyl bromide and 2-bromo-octane. Those compounds with cell dimensions multiples of the simpler values could show varying degrees of optical resolution. The *n*-octyl iodide adduct for which *a* is multiplied seven times contains 49 separate sets of six equivalent molecules. According to space-group symmetry each set of six should have the same configuration, but different sets could be different. Similarly the trigonal adducts such as that with propyl bromide which have doubled *a* dimensions contain four separate sets of six equivalent tri-*o*-thymotide molecules. By measurement of the optical rotatory power of a solution prepared from a single crystal of this adduct, it was found, however, that the resolution was as complete as in the benzene adduct. The crystal contains only one enantiomorphous form of tri-*o*-thymotide molecule and multiplication of cell dimensions is therefore not to be explained by alternations or other sequences of *dextro*- and *lævo*-kinds.

General Conclusions.—Tri-*o*-thymotide has thus been shown to form a hexagonal or trigonal adduct with each of fifty or more substances of varying chemical character all of which have molecules of restricted width. The rules concerning permissible dimensions being known, it is expected that hundreds of other molecules will behave similarly. In particular a large number of long molecules should form the channel type of adduct. An upper limitation of length means that fewer will form the cavity type in which smaller molecules are enclosed as in clathrates. The molecules must also not be too small. One of the enclosable substances, methyl bromide, is a gas at room temperature. Its cavity-type compound decomposes more readily than the others, some of which do not readily lose weight when heated to 100° above the normal boiling point of the included substance. Comparative smallness of the included molecule makes its imprisonment less effective. Attempts to prepare adducts containing yet smaller gas molecules such as argon or carbon dioxide have so far proved unsuccessful.

The results for the whole series have a bearing on a general principle of organic crystal chemistry. The difficulty in finding rules analogous to those applicable for inorganic chemistry is that sufficiently small variations of the structural components cannot usually be made. The effect of varying atomic or ionic radius in simple compounds may be examined by gradual changes, but when naphthalene is compared with benzene, or when two isomers are compared, there are such differences of crystal structure that little information is obtained concerning the factors which influence stability.

In the absence of special complications such as hydrogen-bonding, the molecules in organic crystals pack closely. Not only do neighbouring atoms or groups maintain roughly constant van der Waals equilibrium distances, but also they seem to achieve this in ways that leave no great empty spaces. Kitaigorodski [7] has expressed this by calculating from appropriate atomic radii the volumes proper to certain molecules and comparing them

[7] Kitaigorodski, "Organischeskaya Kristallokhimiya," Acad. Sci., U.S.S.R., Moscow, 1955.

with the volume required for one molecule as calculated from unit-cell dimensions. The result, the packing coefficient of the molecule in the crystal, varies for certain classes of organic compound between 0·6 and 0·8.

Strictly, this coefficient cannot be compared with that for packing of equal spheres. Its value ought to be compared with those for all possible structures of the same substance and, as with spheres, it is probable that many different structures with the same packing coefficient could be devised. That the structure adopted is the closest of all possible packings of the particular assumed molecular shape is improbable in view of the complex nature of molecular interaction, but as a rough guide the close-packing principle may be accepted. In the present work it has been possible to examine the effects of small variations which leave the general character of the structure unchanged. The tendency to close packing is revealed in the minimum of unit cell volume which occurs in the channel-type of adduct whenever possible, but the structure is still formed when less closely packed. Similarly some cavity-type adducts must be less than closest packed since diminution in proper volume of included molecules on substitution of a lower for a higher member of a homologous series is not accompanied by an equal decrease in unit-cell volume.

Experimental

Preparation of Tri-o-thymotide.—Mixtures of tri-*o*-thymotide and di-*o*-thymotide prepared by the method of Wilson Baker, Gilbert, and Ollis [4] were purified by extraction with acetone in a Soxhlet apparatus. In two further extractions, the yield of acetone adduct from the previous stage was used as the starting material. The resulting acetone adduct was twice recrystallised from methanol. The product, which in addition to unsolvated material might contain the methanol adduct, was either heated under reduced pressure or kept at 130° for 24 hr. It was then recrystallised from fractionally distilled *iso*octane in the orthorhombic unsolvated form.

Preparation of Adducts.—Whenever possible the second component material was of " AnalaR " grade. All were further purified by appropriate standard methods. One or two were specimens purified in other laboratories for research purposes. The *n*-pentane was a specimen of purity suitable for mass-spectrometer calibration.

Usually tri-*o*-thymotide was dissolved in the other component heated to a suitable temperature. The solution on cooling deposited a crystalline adduct. In a few cases the nature of the product appeared to depend on the rate of cooling, a more ordered form of adduct resulting from the slower cooling. A few adducts were made by evaporation of solutions at room temperature. Sometimes the crystalline form deposited was metastable and a second form gradually replaced it. When the other component was a solid it was dissolved together with tri-*o*-thymotide in 2 : 2 : 4-trimethylpentane or 2 : 3-dimethylpentane, which do not form adducts. Cooling the solution caused the adduct to crystallise.

Analysis (Chemical).—For many of the compounds carbon and hydrogen percentages are of little value in fixing the ratio of tri-*o*-thymotide to the other component; they are more sensitive mainly when they are not necessary, *i.e.*, when there is a large proportion of halogen. Whenever possible the analysis is based on halogen or active hydrogen which gives a direct determination of the amount of included substance. However, the proportion of active hydrogen is very small and the results will be affected by occluded solvent or moisture, either of which exaggerates the solvent content. Comparatively large amounts of material, 30 mg., were used for active-hydrogen determinations in view of the very small percentage present. A further general difficulty for all chemical methods of analysis arises from decomposition of some adducts and uncertainty concerning methods of drying. For the higher-alcohol adducts prepared by dissolving tri-*o*-thymotide and the alcohol in an indifferent solvent, it seems to be impossible to wash away surplus alcohol without causing decomposition. Although chemical analysis, where its accuracy permits, confirms the compositions given, it is generally unable to provide the finer details required to establish the nature of these molecular compounds. For the alkyl halide cavity-type adducts, apart from that of methyl bromide which is subject to decomposition, a fairly constant value of three molecules per unit cell is found. In these the proportion of halogen is highest and the results are therefore among the more reliable. They agree with the molecular ratio determined from unit-cell weight. For the channel-type adducts chemical analysis shows that in general the molecular proportion of an included substance is

XUM

less the longer its molecules, but the ratio can be determined only roughly in this way. Even in the favourable case of the *n*-pentyl bromide adduct the calculated bromine content changes only from 6·6 to 6·4% when the number of molecules is changed from 3 to 2·9 for each six tri-*o*-thymotide molecules.

Table 4 shows the observed percentages of carbon, hydrogen, halogen, and active hydrogen, as appropriate. Compounds are listed in the same order as in Tables 1 and 2. When no analysis is given the existence of the compound is regarded as established by the *X*-ray investigation. For the cavity-type compounds calculated percentages are based on the composition $2C_{33}H_{36}O_6$,M (M = included molecule). For channel-type adducts calculated percentages are based on the molecular ratios, determined from the unit cell weight as listed in Tables 1 and 2.

TABLE 4.

Included molecule	C (%) Found	C (%) Calc.	H (%) Found	H (%) Calc.	Active H or Halogen (%) Found	Active H or Halogen (%) Calc.
CH_3·OH	74·1	73·7	6·9	7·0	0·09	0·1
C_2H_5·OH	73·9	74·0	6·9	6·9	0·11	0·09
C_3H_7·OH	74·5	74·2	7·3	7·2	0·10	0·09
C_4H_9·OH	74·5	74·9	7·2	7·3	0·10	0·09
C_6H_{13}·OH	—	—	—	—	0·09	0·09
C_7H_{15}·OH	—	—	—	—	0·07	0·08
C_8H_{17}·OH	—	—	—	—	0·07	0·07
$C_{10}H_{21}$·OH	—	—	—	—	0·08	0·06
CH_3Br	70·0	69·9	6·2	6·6	6·1	6·9
CH_3I	67·4	67·1	6·5	6·3	9·9	10·6
C_2H_5Br	70·4	70·0	7·1	6·7	6·9	6·9
C_2H_5I	68·6	67·3	6·2	6·4	10·0	10·5
C_3H_7Br	70·8	69·2	6·7	6·8	6·9	6·8
C_3H_7I	68·3	67·5	6·6	6·5	10·3	10·3
C_4H_9Br	70·5	70·4	6·7	6·8	6·1	6·7
C_4H_9I	68·4	67·7	6·8	6·6	9·7	10·2
$C_5H_{11}Br$	70·7	70·6	7·1	6·9	5·9	7·3
$C_5H_{11}I$	68·1	67·8	6·8	6·7	10·3	10·4
$C_6H_{13}Br$	71·3	71·1	7·1	7·0	5·8	6·0
$C_7H_{15}Br$	72·0	71·6	7·4	6·9	5·5	5·3
$C_7H_{15}I$	70·1	70·6	7·0	6·6	7·3	9·0
$C_8H_{17}Br$	72·5	72·1	6·6	7·1	4·4	4·8
$C_8H_{13}I$ (A)	71·0	70·5	6·8	6·5	7·4	6·8
$C_8H_{13}I$ (B)	70·4	70·5	7·2	6·5	7·3	6·8
$C_{10}H_{22}Br$	73·6	73·6	7·3	6·4	3·3	3·1
$C_{14}H_{33}I$	73·0	73·0	7·3	7·1	4·5	3·4
$C_{18}H_{37}Br$	—	—	—	—	2·0	2·8
$X\cdot[CH_2]_n\cdot X$						
n X						
1 Br	66·1	65·4	6·3	6·1	13·8	13·0
1 I	61·6	60·7	5·76	5·6	19·2	19·2
2 Br	65·8	65·6	6·2	6·2	14·0	12·8
3 Br (A)	70·9	65·8	6·4	6·2	5·8	12·7
3 Br (B)	66·2	65·8	6·5	6·2	13·2	12·7
$Hg(C_2H_5)_2$	63·4	63·9	6·4	6·3	—	—
2-Bromo-octane	71·4	71·7	7·5	7·1	5·0	5·5

Analysis (by Unit-cell Weight).—For a number of adducts the unit-cell weight has been determined accurately. There are 6 molecules of tri-*o*-thymotide of known weight in the cell and the weight of the remainder is determinable. The stated limits of error for molecular ratios are derived from the errors in cell dimensions and densities. Constancy of molecular ratio for the cavity-type, and the consistent relation to molecular length in the channel-type, confirm that this method is much more accurate than chemical analysis.

Determination of Unit-cell Dimensions.—Since owing to the large cell dimensions it would be impossible to index powder photographs, accurate cell dimensions had to be determined by single-crystal methods. Imperfection of the crystals results in vanishingly small intensities of reflexion of Cu radiation at high angles, and accordingly chromium radiation ($\lambda K\alpha_1 = 2{\cdot}2896$, $\lambda K\alpha_2 = 2{\cdot}2935$ Å) was used. The longer wavelength also makes for more certain indexing. A Unicam oscillation camera was used with film mounted according to Straumanis's method. Oscillation about the *c*-axis does not require an estimate of the axial ratio *c*/*a*, but there were no reflexions suitable for accurate extrapolation in either the cavity- or the channel-type crystals.

Oscillation about the *a*-axis was sometimes employed but usually both *a* and *c* were obtained from photographs made by oscillation about [210]. By suitable selection of oscillation ranges photographs symmetrical to right and left were obtained, and the points of entrance and exit of *X*-ray beam could be determined. Films were measured on a universal instrument of the Cambridge Instrument Company. Values of the Bragg *d*-spacings for a series of high-angle reflexions were extrapolated against $\sin^2\theta$ for values of θ above 70°. Some cell constants were obtained from Weissenberg films calibrated with the lines of metallic palladium. The palladium specimen was one used by Hume-Rothery and Hellawell [8] who determined its lattice constant as 3·8908 Å. Apart from the accurate cell dimensions needed to establish the rules of composition in the two main series of the adducts a number of approximate cell constants, derived from oscillation photographs taken with Cu-K_α or Cr-K_α radiation, are recorded in Table 1 in order to show the type of adduct formed by molecules of different lengths. For these no temperature is given.

Density Measurements.—Gradient columns were made with aqueous solutions of sodium bromide and calibrated with drops of xylene–bromobenzene mixtures. Densities of the mixtures were determined in a pyknometer. A column method is dictated by the small quantities of material available and the possible decomposition of some adducts. It has the advantage of showing by the sharpness of the layers formed in the column that in nearly all cases, the compositions are definite. In several instances it revealed a mixed product of two different crystalline forms which separated into two layers in the column. Thus both densities could be determined. Freshly prepared material was dried at the pump. If it was an adduct of a high-boiling substance it was washed with light petroleum to remove any adhering second component. A small quantity was powdered and covered with solution similar to that in the column, sometimes with the addition of a little wetting agent. It was kept in a vacuum-desiccator for ½ hr., then washed into the column below the surface. Sharp layers of powder were obtained with some scattered fragments above consisting of less dense material presumably containing air. Positions of the calibrating drops and the position and spread of the layers were read with a cathetometer. An accuracy better than 1 : 1000 was usually obtained for the density.

In a few instances no density is recorded because a sharp layer could not be obtained in the density gradient column, or because little more than a single crystal of an adduct had been obtained and attempted repetition of the preparation gave a different crystalline form.

Molecular Weights.—The unit-cell weights are expressed in terms of O = 16·000 and are based on the unit-cell dimensions and the densities given in the Tables. Densities were measured at 20° and most cell constants within a degree or two of that temperature. Cell dimensions measured over a range of temperature for the ethanol and heptyl bromide adducts give the following changes (Å) of lattice constant for one degree rise of temperature: ethanol adduct, +0·001 (*a*), +0·0017 (*c*); heptyl bromide adduct, +0·0017 (*a*), −0·0006 (*c*). Where necessary, cell dimensions were corrected to 20° on the supposition that the two sets of values given above would hold for other crystals of the cavity and the channel type respectively. The value of Avogadro's number appropriate to cell dimensions in Ångström units was taken as $0{\cdot}60236 \times 10^{24}$. This is the value derived, after allowance for the conversion into the chemical scale of atomic weights, from a 1955 adjustment [9] of atomic constants and agrees with that obtained by Batuecas [10] from diamond. The weight of six molecules of tri-*o*-thymotide based on C = 12·01 and H = 1·008 is 3171·7 and for a typical case, that of the propan-1-ol adduct, the total cell weight is 3350·8. It is the difference, 179·1, divided by the molecular weight of propanol which gives the number of included molecules per unit cell and the accuracy of this result depends on that of the total cell weight. To show the kind of deviation from rational formula that may occur in the channel compounds it is necessary to estimate this difference to within 1—2%, *i.e.*, about 3 units of weight. Hence the total cell weights have been determined to approximately one part in a thousand. Atomic weights of comparable accuracy have to be used as may be seen in the example.

CHEMICAL CRYSTALLOGRAPHY LABORATORY,
SOUTH PARKS ROAD, OXFORD.

[*Received, February 4th*, 1958.]

[8] Hume-Rothery and Hellawell, personal communication.
[9] Cohen, DuMond, Layton, and Rollett, *Rev. Mod. Phys.*, 1955, **27**, 363.
[10] Batuecas, *Nature*, 1950, **165**, 61.

XUM

472. *Structure of the Capsular Polysaccharide of* Aerobacter aerogenes (*N.C.T.C.* 418).

By S. A. Barker, A. B. Foster, I. R. Siddiqui, and M. Stacey.

The capsular acidic polysaccharide of *Aerobacter aerogenes* (N.C.T.C. 418) has been shown to contain D-glucose, D-mannose, glucuronic acid, and probably mannuronic acid. Partial acidic hydrolysis of the polysaccharide gave *inter alia* two aldobiuronic acids which were assigned the structures 4-*O*-α-D-glucuronosyl-D-mannose and 4-*O*-α-D-mannuronosyl-D-glucose. Hydrolysis of the methylated polysaccharide gave 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose, 2·3%; 2 : 3 : 4-tri-*O*-methylglucuronic acid, 2·6%; tri-*O*-methylhexoses, 90% and di-*O*-methylhexoses (mainly 2 : 6-di-*O*-methyl-D-mannose), 5·1%. Two of the tri-*O*-methylhexoses were shown to be 2 : 3 : 6-tri-*O*-methyl-D-glucose and 2 : 4 : 6-tri-*O*-methyl-D-glucose.

Few detailed chemical studies have been made on the capsular polysaccharides elaborated by the many serologically distinguishable strains [1] of the *Aerobacter–Klebsiella* group. The capsular polysaccharides corresponding to *Klebsiella* types 1, 2, and 3 have been examined by Heidelberger, Goebel, and Avery,[2] Goebel and Avery,[3] and Goebel [4] who found them to be glucose-containing polyuronides. More recently Wilkinson, Dudman, and Aspinall [5] have shown that *Klebsiella* type 54 elaborated a polyuronide consisting of D-glucose (50%), L-fucose (10%) and an unidentified uronic acid (29%). Dudman and Wilkinson [6] also slowed that the polysaccharides of *Klebsiella* types 8, 26, 29, and 57 contained varying proportions of galactose, mannose, and uronic acid; types 8 and 26 contained glucose in addition. The present communication deals with a structural study of the capsular acidic polysaccharide produced by the Hinshelwood strain of *Aerobacter aerogenes* obtained from the Oxford University Physical Chemistry Laboratory and later found to be identical with N.C.T.C. 418.

A large-scale culture (500 l.) of the Hinshelwood strain, in a synthetic medium containing mineral salts and glucose as the sole source of carbon, gave enough acidic polysaccharide for most of the structural determination. The major step in the purification of the polysaccharide involved the use of " Cetavlon " [7] since this precipitated a mixture of nucleic acid and acidic polysaccharide and left in solution small amounts of neutral polysaccharide. Paper chromatography of a hydrolysate of the neutral polysaccharide indicated that its major constituent was glucose with small amounts of galactose. The cetyltrimethylammonium salts of the nucleic acid and the acidic polysaccharide mixture were separated by differential solubility in 0·25M-sodium chloride.

A purified sample of the acidic polysaccharide (Na salt) had $[\alpha]_D^{21}$ +97·3° and was electrophoretically pure except for a small amount (3·5%) of nucleic acid impurity. Paper chromatography and ionophoresis [8] of a hydrolysate showed glucose, mannose (*ca.* 3 : 1), glucuronic acid, and aldobiuronic acids. The acidic polysaccharide had a uronic acid content of 16·5% when analysed by the McCready, Swensen, and Maclay [9] method modified to enable determinations to be carried out on 20 mg. samples. (Control determinations on samples of crystalline glucurone gave reproducible recoveries of 101·2%.) Confirmation of the presence of carboxylic acid groupings was obtained from the infrared spectrum [10]

[1] Edwards and Fife, *J. Infect. Diseases*, 1952, **91**, 92.
[2] Heidelberger, Goebel, and Avery, *J. Exp. Med.*, 1925, **42**, 701.
[3] Goebel and Avery, *ibid.*, 1927, **46**, 601.
[4] Goebel, *J. Biol. Chem.*, 1927, **74**, 619.
[5] Wilkinson, Dudman, and Aspinall, *Biochem. J.*, 1955, **59**, 446.
[6] Dudman and Wilkinson, *Biochem. J.*, 1956, **62**, 289.
[7] Jones, *Biochim. Biophys. Acta*, 1953, **10**, 607.
[8] Foster, *J.*, 1953, 982.
[9] McCready, Swensen, and Maclay, *Ind. Eng. Chem.*, 1946, **18**, 290.
[10] Barker, Bourne, and Whiffen, " Methods of Biochemical Analysis," Interscience, New York, Vol. 3, 1956, p. 213.

of the acidic polysaccharide. The spectrum of the sodium salt showed strong absorption at 1612 cm.$^{-1}$ and 1410 cm.$^{-1}$ characteristic of the carboxylate ion. No amide bands (C=O, 1650 cm.$^{-1}$ and $-$NH, 1550 cm.$^{-1}$) such as those given by proteins or analogous to those displayed by an *N*-acetyl group could be detected. The absence of absorption at 1735 cm.$^{-1}$ in the spectrum of the sodium salt also indicated the absence of *O*-acetyl groups. However, absorption did appear in the spectrum of the free acid attributable to the C=O of the un-ionised $-CO_2H$ group. No attempt was made to interpret the region 700—1000 cm.$^{-1}$ since the α- and β-configurations of the hexose units cannot be deduced in the presence of uronic acids which show interfering absorption in this region.

The mixture of saccharides produced by partial hydrolysis of the acidic polysaccharide was fractionated (without prior neutralisation) on a charcoal–Celite column.[11] The major fraction (A) eluted with water was found to contain mainly glucose and mannose when analysed by paper chromatography. Further elution with water, and gradient elution [12] with aqueous ethanol (0 ⟶ 20%), gave fractions B and C containing the barium and the sodium salt respectively of glucuronic acid together with traces of another hexuronic acid, and fraction D, an aldobiuronic acid mixture.

The components of fraction A were separated by preparative paper chromatography and the glucose was characterised as crystalline *N*-*p*-nitrophenyl-β-D-glucopyranosylamine dihydrate,[13] and the mannose as *N*-*p*-nitrophenyl-β-D-mannopyranosylamine dihydrate.[13] The two *p*-nitroanilides showed a large difference in their solubility in methanol, and in fact a mixture of glucose and mannose may be separated readily by conversion into the *p*-nitroanilides.

The two hexuronic acid fractions B and C were converted into their methyl ester methyl hexuronosides. Reduction with lithium aluminium hydride [14–16] and acidic hydrolysis of the resulting methyl hexosides gave glucose and small amounts of mannose. This indicated the presence of both glucuronic and mannuronic acid in the acidic polysaccharide.

Paper chromatography indicated the presence of two aldobiuronic acids in fraction D and these were separated on sheets of Whatman No. 1 paper. An acidic hydrolysate of the component (1) with lower R_F value was analysed and showed the production of glucose and a component suspected to be mannuronic acid. Similar treatment of the faster moving component (2) gave mannose and glucuronic acid. Each aldobiuronic acid was converted into its methyl ester methyl glycoside and reduced with lithium aluminium hydride.[14–16] Chromatography of the hydrolysates of the resulting methyl biosides showed the presence of equal amounts of glucose and mannose in each case. This evidence, together with the acid stability of the aldobiuronic acids, indicated that component 1 was a glucuronosyl-mannose and component 2 a mannuronosyl-glucose. Periodate oxidation of the methyl biosides obtained by reduction from fraction D consumed 3 moles of periodate and produced 1·1 moles of formic acid per 356 g. of methyl biosides. No formaldehyde could be detected and a minute amount (*ca.* 2·5%) of mannose was produced on acid hydrolysis of the periodate-oxidised methyl biosides. This evidence indicated that no furanoside ring was present, that only a minute amount of the methyl biosides could be linked through the 3 position, and that the major portion were linked 1 : 4 or 1 : 2.

In order to decide between these possibilities the same methyl bioside fraction was methylated [17] three times with methyl sulphate–sodium hydroxide and once with the Purdie reagents. Acidic hydrolysis of the product gave approximately equal amounts of components having the mobilities of tetra-*O*-methylmannose (or -glucose) and tri-*O*-methylhexoses respectively. When these products were eluted from paper and submitted

[11] Whistler and Durso, *J. Amer. Chem. Soc.*, 1950, **72**, 677.
[12] Alm, Williams, and Tiselius, *Acta Chem. Scand.*, 1952, **6**, 826.
[13] Perkow, Kuhner, and Weygard, *Chem. Ber.*, 1951, **84**, 594.
[14] Lythgoe and Trippete, *J.*, 1950, 1983.
[15] Akher and Smith, *Nature*, 1950, **166**, 1037.
[16] Whistler and Hough, *J. Amer. Chem. Soc.*, 1954, **76**, 1670.
[17] Albon, Bell, Blanchard, Gross, and Rundell, *J.*, 1953, 24.

to paper ionophoresis [8] in borate buffer of pH 10, no components could be detected having the mobilities of the 3 : 4 : 6-tri-*O*-methyl ether of either mannose or glucose. This indicated the absence of 1 : 2-linkages in the methyl biosides and hence in the aldobiuronic acids. From the methylation and periodate data it therefore appears that the aldobiuronic acids are 1 : 4-linked.

The high specific rotation (+97·3°) of the acidic polysaccharide indicated a high percentage of α-linkages. Several observations suggested that α-linkages were present in the aldobiuronic acids. Both the aldobiuronic acid mixture (fraction D) and the mixture of methyl biosides derived therefrom were resistant to emulsin; this indicated the absence of β-linkages. The action of α-glucamylase on the methyl biosides, reputedly [18] specific for α-1 : 4-glucose residues, gave small amounts of glucose and mannose.

The acidic polysaccharide gave precipitates in varying amounts with several types of anti-*Pneumococcus* horse sera; the strongest reactions were given with antisera to Types II and XV. Only the structure [19] of the Type II *Pneumococcus* polysaccharide is known. Since Type II *Pneumococcus* polysaccharide only contains D-glucose, D-glucuronic acid, and L-rhamnose, the strong cross-reaction must be due to a similarity of linkage of the glucose residues (which are involved in 1 : 4 : 6-branch points), the glucuronic acid residues, or both. It has already been demonstrated [20,21,22] that the cross-reaction of anti-*Pneumococcus* Type II serum with certain dextrans, amylopectins, etc., is probably due to glucose in 1 : 4 : 6-branch points, and that with gum arabic to the similar disposition of D-glucuronic acid residues. It is significant that the *Aerobacter aerogenes* polysaccharide failed to cross-react with Type I anti-serum; the specific polysaccharide of Type I contains galacturonic acid.[23]

On periodate oxidation the acidic polysaccharide consumed 0·98, 1·15, 1·22, and 1·27 moles of periodate per 162 g. of polysaccharide after oxidation for 48, 72, 96, and 112 hr. respectively. The values for formic acid after the same times expressed as moles per 162 g. of polysaccharide were 0·55, 0·65, 0·71, and 0·74. Recent work by Eddington, Hirst, and Percival [24] on the periodate oxidation of methyl ethers of glucuronic acid suggests that owing to the possibility of over-oxidation considerable caution should be exercised in interpreting periodate data of polysaccharides containing uronic acids. Over-oxidation is the probable explanation of the high ratio of acid produced to periodate consumed by the acidic polysaccharide. From the work of Eddington *et al.*[24] it appears that such over-oxidation is to be expected where the uronic acids are present as non-reducing terminal units or where they are linked through the 2-position. We can, however, deduce that the maximum number of residues in the acidic polysaccharide which could be linked 1 : 6 or be present as non-reducing terminal units is 63%. This leaves a minimum of 37% of the residues which are linked 1 : 3 or are involved in branching. Acid hydrolysis of the periodate-oxidised acidic polysaccharide revealed appreciable amounts of glucose and mannose, indicating that only these hexose moieties could be included in those residues resistant to periodate oxidation and so in the figure of 37%.

Since the acidic polysaccharide prepared in 500 l. of medium was then exhausted an attempt was made to prepare more polysaccharide. However, with both our culture and a fresh slope sent from Oxford University Physical Chemistry Laboratory only minute amounts of the polysaccharide were produced. Fortunately, Professor Sir Cyril Hinshelwood had many years previously sent a culture of this strain to the National Collection of Type Cultures (there designated N.C.T.C. 418). With this culture success was immediately obtained.

[18] Barker, Bourne, and Fleetwood, *J.*, 1957, 4865.
[19] Butler and Stacey, *J.*, 1955, 1537.
[20] Heidelberger and Aisenberg, *Proc. Nat. Acad. Sci.*, 1953, **39**, 453.
[21] Heidelberger, Aisenberg, and Hassid, *J. Exp. Med.*, 1954, **99**, 343.
[22] Heidelberger and Adams, *ibid.*, 1956, **103**, 189.
[23] Heidelberger, *ibid.*, 1936, **64**, 559.
[24] Eddington, Hirst, and Percival, *J.*, 1955, 2281.

By using the N.C.T.C. strain and the medium employed by Duguid and Wilkinson [25] more acidic polysaccharide (3·4 g.) was isolated from the capsules of the organisms. The polysaccharide thus obtained appeared to be identical with the previous polysaccharide on the basis of paper chromatographic and ionophoretic examination of its hydrolysate.

The acidic polysaccharide was methylated with sodium and methyl iodide in liquid ammonia and after four methylations, each involving four alternate additions of the methylating reagents, a methyl ether was obtained having $[\alpha]_D^{16}$ +65·6° in $CHCl_3$ and OMe, 40%.

The infrared spectra of the methylated polysaccharide, as isolated, showed no absorption at 1730—1760 cm.$^{-1}$ (C=O stretching), indicating the absence of CO_2Me and un-ionised CO_2H groups. However an absorption peak at 1635 cm.$^{-1}$ indicated the presence of a carbonyl group of CO_2Na, CO_2NH_4 or $CO{\cdot}NH_2$, and/or water. The free acid form of the methylated polysaccharide showed a peak at 1730—1735 cm.$^{-1}$ and hence the presence of free CO_2H groups. This evidence clearly shows that none of the carboxylic acid groups was esterified during methylation and most were isolated in the form of an ionizable salt. Finally, from the intensity of the OH stretching band the estimated amount of free hydroxyl groups in the methylated polysaccharide could not be more than 5%.

The methylated polysaccharide was subjected to methanolysis and hydrolysis, and the hydrolysate separated into neutral and acidic fractions on an anion-exchange resin [26] (Deacidite FF, micro-bead, carbonate form). The neutral methyl sugars were further separated into di-*O*-methyl-, tri-*O*-methyl-, and tetra-*O*-methyl-hexose fractions, by using paper chromatograms.

The syrupy tetra-*O*-methylhexose fraction showed $[\alpha]_D^{20}$ +66° [cf. 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose, +84° (equil.); 2 : 3 : 4 : 6-tetra-*O*-methyl-D-mannose, +1·2° (equil.)]. The component behaved in an identical manner to 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose on paper chromatography and its infrared spectrum was identical with that of an authentic sample of 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose eluted from the paper under similar conditions. This evidence showed that some of the glucose residues were present as non-reducing end groups in the acidic polysaccharide, and the amount of 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose isolated indicated such residues constituted *ca.* 1 in 44 sugar units.

The di-*O*-methyl fraction showed $[\alpha]_D^{20}$ +9·1° in H_2O. On demethylation [27] it gave, *inter alia*, mainly mannose with very small amounts of glucose. Paper ionophoresis [8] revealed the presence of a major component (M_G 0·092) with minute traces of two other components having M_G values identical with those of 2 : 3- and 2 : 4-di-*O*-methylglucose. The major component (M_G 0·092) was shown, by comparison with authentic samples, to differ from 2 : 4-, 2 : 3-, 3 : 4-, 3 : 6-, and 4 : 6-di-*O*-methylglucose and 2 : 3-, 3 : 4-, and 4 : 6-di-*O*-methylmannose. This di-*O*-methyl fraction was reduced with sodium borohydride, and the resulting di-*O*-methylhexitol subjected to periodate oxidation. It consumed 1·9 moles of periodate and produced 0·9 mole of formic acid per mole; no formaldehyde was detected. These periodate data strongly indicate a 2 : 6-di-*O*-methylhexitol.

The low optical rotation of the di-*O*-methylhexose fraction {$[\alpha]_D^{20}$ +9·1° compared with $[\alpha]_D$ +63·3° (equil.) for 2 : 6-di-*O*-methyl D-glucose [28]} strongly suggests that the major di-*O*-methylhexose is 2 : 6-di-*O*-methyl-D-mannose. Such moieties would arise from the branch points in the acidic polysaccharide and would constitute (from the amount isolated) *ca.* one in twenty of the sugar residues. The presence of 2 : 6-di-*O*-methylmannose accounts for at least some of the mannose residues that were resistant to periodate oxidation in the acidic polysaccharide.

[25] Duguid and Wilkinson, *J. Gen. Microbiol.*, 1953, **9**, 174.
[26] Machell, *J.*, 1957, 3389.
[27] Hough, Jones, and Wadman, *J.*, 1950, 1702.
[28] Freudenberg and Hüll, *Ber.*, 1941, **74**, 237.

XUM

The methylated uronic acid fraction showed on' one reducing component on paper chromatography and this had an R_F value and stain. g properties identical with those of 2 : 3 : 4-tri-*O*-methylglucuronic acid. However, after reduction with lithium aluminium hydride, hydrolysis, and paper chromatography, one spot was detected having an R_F value and staining properties identical with those of 2 : 3 : 4-tri-*O*-methylglucose and another had those of the 2 : 6-di-*O*-methylmannose reported above. The infrared spectrum of the 2 : 3 : 4-tri-*O*-methylglucose isolated from a paper chromatogram was identical with that of an authentic specimen eluted from the paper in a similar way. This evidence indicated the presence of non-reducing end groups of glucuronic acid and the amount of tri-*O*-methylglucuronic acid isolated corresponded to *ca.* 1 in every 40 sugar units.

The detection of 2 : 6-di-*O*-methylmannose in the hydrolysate of the reduced methylated uronic acid fraction suggested the presence of small amounts of the methyl glycoside of a methylated aldobiuronic acid. This inference was supported by the fact that a 2 : 6-di-*O*-methyl-sugar could not result from the reduction of a di-*O*-methylhexuronic acid and also by the evidence that the unreduced methylated uronic acid fraction on rehydrolysis, followed by paper chromatography and ionophoresis of the hydrolysate, showed, in addition to 2 : 3 : 4-tri-*O*-methylglucuronic acid, a dimethyl component having an M_G value identical with that of 2 : 6-di-*O*-methylmannose. It is therefore inferred that some at least of the glucuronic acid end groups are linked to mannose residues engaged in branching.

The tri-*O*-methylhexose fraction was found on ionophoresis to contain neither 3 : 4 : 6-tri-*O*-methylglucose nor 3 : 4 : 6-tri-*O*-methylmannose, thus ruling out the possibility of 1 : 2-linkages. The mixture of tri-*O*-methylhexitols obtained on reduction of this fraction consumed 0·96 mole of periodate per mole and produced no formic acid. This evidence precluded the presence of large amounts of 2 : 4 : 6-tri-*O*-methylhexoses and favoured the presence of either 2 : 3 : 6- or 2 : 3 : 4-tri-*O*-methyl ethers.

Partial separation of the tri-*O*-methylhexose fraction was effected on paper chromatograms into A (slower components) and B (faster components). A showed $[\alpha]_D^{20}$ +36·4° (in H_2O) and on demethylation [27] gave, *inter alia*, both glucose and mannose. When treated with aniline in methanol, A gave a very small yield of crystalline 2 : 4 : 6-tri-*O*-methyl-*N*-phenyl-D-glucosylamine. B showed $[\alpha]_D^{20}$ +45° (in H_2O) and on demethylation [27] gave, *inter alia*, mainly glucose with comparatively small amounts of mannose. In order to decide whether any 2 : 3 : 6-tri-*O*-methylglucose was present in the mixture it was kept in 2% dry methanolic hydrogen chloride at room temperature. It showed $[\alpha]_D^{22}$ +50·7° (10 min.) ⟶ +7·2° (24 hr., equil.). Paper chromatographic comparison of solutions of B before and after the treatment with methanolic hydrogen chloride showed almost complete disappearance of the faster region of the spot (R_F identical with that of 2 : 3 : 6-tri-*O*-methyl-D-glucose). It is known [29] that under these conditions 2 : 3 : 6-tri-*O*-methyl-D-mannose does not form a furanoside. It is concluded that the major component of B is 2 : 3 : 6-tri-*O*-methyl-D-glucose.

It is concluded that the polysaccharide has a branched structure in which the average repeating unit is about 40 sugar units and contains D-glucose and D-mannose residues with some of the former present as non-reducing end groups. The D-glucose residues are linked mainly 1 : 4 but a few are linked 1 : 3. Non-reducing end groups (*ca.* 1 in 40) of glucuronic acid are linked α-1 : 4 to D-mannose residues, which in turn are linked to the remaining sugar units through the 3-position. The linkage of the remaining mannose residues in the repeating unit has still to be determined but is through the 4- or the 6-position. The first batch of acidic polysaccharide showed a higher uronic acid content (16·5%) than the second (2·6%), probably because of the use of different culture media. In the first batch, mannuronic acid residues were detected and these were attached α-1 : 4 to D-glucose residues.

[29] Rebers and Smith, *J. Amer. Chem. Soc.*, 1954, **76**, 6097.

Experimental

Isolation of Acidic Polysaccharide.—Aqueous solutions containing glucose (194 l.; 50 g./l.), $(NH_4)_2SO_4$ (97 l.; 5 g./l.), $MgSO_4,7H_2O$ (9 l.; 1 g./l.) together with a phosphate buffer (194 l.; pH 7—7·2) made from Na_2HPO_4 (17·3 g./l.) and KH_2PO_4 (2·7 g./l.) were sterilised separately at 10 lb./sq. in. for 5 min., mixed, and then steamed for 20 min. at 100°. After cooling, the medium was inoculated with a culture (6 l.) of *Aerobacter aerogenes* (Oxford University Physical Chemistry Laboratory strain) prepared by growing the organism for 18 hr. on a medium with the same composition as that described above. This large-scale culture was kindly grown for us at the Antibiotics Research Station, Clevedon, where it was incubated for 48 hr. at 37° with aeration. The cells were harvested by means of a Sharples Super Centrifuge, frozen, and then disrupted with the aid of glass beads. The cell debris was removed by centrifugation, and the nucleic acid and acidic polysaccharide in the extract were precipitated by addition of excess of Cetavlon. The precipitate was dissolved in M-sodium chloride, then diluted with water until 0·25M with respect to sodium chloride. The resulting nucleic acid precipitate was centrifuged off and the crude acidic polysaccharide precipitated from the supernatant liquid by addition of alcohol (3 vol.). The precipitate was removed in the centrifuge and dried with alcohol and ether (yield, 13 g.).

Cultures from the above strain two years later had become " rough " and produced only minute amounts of acidic polysaccharide. Subcultures from a slope of the same strain sent many years previously to the National Collection of Type Cultures (there designated N.C.T.C. 418) were used to produce two further 20 l. batches, yielding 3·4 g. of acidic polysaccharide. A similar procedure was adopted but the medium used was obtained by mixing aseptically aqueous solutions, each 5 l., containing (i) Na_2HPO_4 (200 g.) and KH_2PO_4 (60 g.), (ii) $(NH_4)_2SO_4$ (6 g.), K_2SO_4 (20 g.), $MgSO_4,7H_2O$ (4 g.) and $FeSO_4,7H_2O$ (0·2 g.), (iii) NaCl (20 g.) and $CaCl_2$ (0·2 g.), (iv) glucose (200 g.) which were sterilised separately at 10 lb./sq. in. for 10 min.

Further purification of the acidic polysaccharide was effected by deproteinising it (Sevag [30] method) several times with chloroform–pentyl alcohol (9 : 1), reprecipitating it with Cetavlon, and fractionating it, as above, with sodium chloride.

One fraction, so purified, had $[\alpha]_D^{20}$ +97·3° (*c* 0·339 in N-sodium hydroxide) and analysis showed: C, 35·9; H, 6·5; N, 1·4; P, 0·5%. The optical density at 260 mμ corresponded to a maximum nucleic acid impurity of 3·5%. Uronic determination, by a modification of the McCready, Swensen, and Maclay method,[9] showed a uronic acid content of 16·5%. The fraction gave 1·69% of ash. On analysis of the fraction in a Tiselius electrophoresis apparatus, using a 0·05M-borate buffer (pH 9·2), only one major component could be detected and corresponded to the polysaccharide. A very small faster-moving component corresponded to the nucleic acid impurity.

Infrared Spectra of Acidic Polysaccharide.—The infrared absorption spectra of the acidic polysaccharide were determined as the sodium salt and free acid at two concentrations (0·375 mg./cm.^{2} and 1·5 mg./cm.^{2}) in potassium chloride discs. The polysaccharide was obtained in the free acid form by precipitation of the polysaccharide (50 mg.) from acid solution (pH 1·2) with alcohol (3 vol.), dialysis of an aqueous solution of the precipitate, and freeze-drying.

Periodate Oxidation of Acidic Polysaccharide.—The polysaccharide was subjected to periodate oxidation by the procedure of Jeanes and Wilham [31] which incorporates Fleury and Lange's method [32] for the determination of the quantity of periodate consumed, and that of Halsall, Hirst, and Jones,[33] with certain modifications, for the determination of formic acid produced. The number of moles of sodium periodate consumed per 162 g. of polysaccharide was: 48 hr., 0·98; 72 hr., 1·15; 96 hr., 1·22; 112 hr., 1·27. The corresponding figures for formic acid produced were: 48 hr., 0·55; 72 hr., 0·65; 96 hr., 0·71; 112 hr., 0·74.

The solution (50 ml.) remaining from the oxidation of the polysaccharide was dialysed for 4 days against running tap-water and then freeze-dried. This material was then hydrolysed with 2N-sulphuric acid (1 c.c.) for 3 hr. at 100°. After neutralisation with barium carbonate the hydrolysate was submitted to paper chromatography with butan-1-ol–acetic acid–water (4 : 1 : 5) and found to contain glucose and mannose but no uronic acids.

[30] Sevag, *Biochem. Z.*, 1934, **273**, 419.
[31] Jeanes and Wilham, *J. Amer. Chem. Soc.*, 1950, **72**, 2655.
[32] Fleury and Lange, *J. Pharm. Chim.*, 1933, **17**, 107, 196.
[33] Halsall, Hirst, and Jones, *J.*, 1947, 1427.

XUM

Immunological Specificity of Acidic Polysaccharide (with Professor M. HEIDELBERGER).—The polysaccharide (0·06 mg. in 0·04 c.c. of physiological saline) cross-reacted with the following anti-*Pneumococcus* serums after being kept at 0° for 8 days.

Type	II	VII	IX	X	XII	XV	XVIII	XIX	XX
Reaction ...	++++	+	++	+	±	++++	+	++	+±

Partial Hydrolysis of Acidic Polysaccharide.—The polysaccharide (2·5 g.) was hydrolysed with 2N-sulphuric acid (75 c.c.) under nitrogen for 3 hr. at 100°. The hydrolysate (without neutralisation) was added to a charcoal–Celite column (l, 24 cm.; diam. 3 cm.) and fractionated by Whistler and Durso's method.[11] The column was washed with water, and the effluent collected (19 × 50 c.c. fractions), neutralised with barium carbonate, centrifuged, and concentrated *in vacuo*. Thereafter the column was washed by gradient elution with aqueous ethanol (0 ⟶ 20%; 3 l.), and the fractions (50 c.c.) were neutralised with sodium hydroxide. After paper chromatography with the solvent used above the fractions were grouped as follows: A (1—13) contained 0·66 g. of a glucose, mannose, ribose (*ca.* 3 : 1 : trace) mixture; B (14—19) and C (20—40) contained 25 mg. and 55 mg. respectively of the barium and sodium salt of glucuronic acid together with traces of another hexuronic acid; D (45—54) contained two components (400 mg.), suspected of being aldobiuronic acids, which were separable after lengthy irrigation in the above solvent.

(i) *Fraction A.* A portion of this fraction, after methanol-extraction, was separated into bands on 8 sheets of Whatman No. 1 paper (46 × 57 cm.) and irrigated with the above solvent for 5 days. Elution with water of the appropriate strips gave glucose (0·18 g.) and mannose (0·08 g.). The glucose fraction was purified by repeated extraction with methanol, and the resulting syrup (80 mg.) refluxed for 15 min. with an aliquot part (2 c.c.) of a solution containing *p*-nitroaniline (9 g.), methanol (200 c.c.), and concentrated hydrochloric acid (0·14 c.c.). The mixture was filtered while hot and on cooling gave a solid which after two recrystallisations (yield, 30 mg.) showed $[\alpha]_D^{19}$ −194° (3 min.) ⟶ −201° (equil.) (*c* 1·0 in pyridine) and had m. p. 184° undepressed on admixture with *N*-*p*-nitrophenyl-β-D-glucopyranosylamine,$2H_2O$. The mannose fraction was freed from impurities as above and the resulting syrup (40 mg.) refluxed for 15 min. with *p*-nitroaniline solution (2 c.c.). Deep yellow crystals, which separated from the hot solution, were washed with hot methanol and dried (yield, 8 mg.). The crystals showed $[\alpha]_D^{19}$ −402° (3 min.) ⟶ −332° (equil.) (*c* 0·1 in dry pyridine) and had m. p. 219° undepressed on admixture with *N*-*p*-nitrophenyl-β-D-mannopyranosylamine,$2H_2O$.

(ii) *Fractions B and C.* Fraction B (25 mg.) was refluxed with 2% methanolic hydrogen chloride (1 c.c.) for 6 hr. Part of the hydrogen chloride was removed *in vacuo* by repeated distillation with methanol, and the remainder in a vacuum-desiccator over solid potassium hydroxide. The residue was dissolved in tetrahydrofuran (4 c.c.)–ether (1 c.c.) and reduced with excess of lithium aluminium hydride (*ca.* 100 mg.), added in small amounts during 1 hr., at room temperature. After a further 1 hour's stirring, the reaction was completed at 80° (0·5 hr.). The excess of lithium aluminium hydride was decomposed with water, the suspension was filtered, the residue was extracted twice with water, and the combined filtrates were de-ionised with Amberlite IR-120 and IR-4B resins. The resulting methyl hexoside was hydrolysed with 2N-sulphuric acid (0·5 c.c.) at 100° for 3 hr. Paper chromatography of the neutralised hydrolysate showed the presence of glucose with traces of mannose. Fraction C, submitted to the same reduction and hydrolysis, gave a solution which contained glucose with small amounts of mannose.

(iii) *Fraction D.* A portion (60 mg.) of fraction D was separated on two sheets of Whatman No. 1 paper (46 × 57 cm.) irrigated with the butanol–acetic acid solvent for 10 days. After extraction of the appropriate strips with water and concentration *in vacuo* the yields obtained were slower-moving aldobiuronic acid (0·020 g.) (component 1) and faster-moving aldobiuronic acid (0·026 g.) (designated component 2).

Portions (5 mg.) of component 1, component 2, and the original mixture fraction D were each hydrolysed with 2N-sulphuric acid (0·5 c.c.) at 100° for 3 hr. Paper chromatography of the neutralised hydrolysates showed: component 1 hydrolysate contained glucose, mannuronic acid (?), and unhydrolysed component 1; component 2 hydrolysate contained mannose, glucuronic acid, and unhydrolysed component 2; fraction D hydrolysate contained glucose, mannose (*ca.* 1 : 3), glucuronic acid, mannuronic acid (?), and unhydrolysed aldobiuronic acids.

The methyl ester methyl glycosides of component 1 (15 mg.), component 2 (20 mg.), and

the original mixed fraction D (20 mg.; 300 mg.) were each reduced with lithium aluminium hydride by the same procedure used for fraction B. All the products were non-reducing. Part of the methyl biosides was retained for further examination (see below) while the remainder was hydrolysed with 2N-sulphuric acid at 100° for 3 hr. Paper chromatography of the hydrolysates of reduced component 1, reduced component 2, and the reduced mixed fraction D showed that each contained glucose and mannose in approximately equal quantities.

The aldobiuronic mixture, fraction D (4 mg.), was incubated at 30° for 4 days with emulsin (4 mg. in 0·25 c.c.). A control containing cellobiose (4 mg.) in place of fraction D was incubated simultaneously. Aliquot portions were withdrawn at intervals of 24, 48, 72, and 96 hr. and examined by paper chromatography in the butanol–acetic acid solvent. Cellobiose was progressively broken down to glucose, but the aldobiuronic acid fraction remained unaffected. The methyl biosides obtained by reduction of fraction D were also stable to emulsin. The same methyl biosides (4 mg.) were incubated at 30° for 4 days with α-glucamylase (4 mg. in 0·25 c.c.). A control solution containing maltose (4 mg.) was incubated simultaneously. Paper chromatography showed the progressive formation of glucose from maltose, and small amounts of glucose and mannose from the methyl biosides.

Methyl biosides (27·8 mg.) obtained by reduction of fraction D were oxidised with 0·15M-sodium periodate (25 c.c.). The consumption of periodate and production of formic acid (expressed as moles per 356 g. of methyl biosides) were 3 and 1·1 respectively. No formaldehyde was detected. Acid hydrolysis of the remaining periodate-oxidised methylbiosides and semiquantitative paper chromatography showed that only *ca.* 2·5% of mannose was produced.

The methyl bioside(s) (40 mg.) obtained by reduction of fraction D were methylated [17] in dioxan (4 c.c.) by alternate additions of dimethyl sulphate (3·6 c.c.) and 30% sodium hydroxide (7·2 c.c.) in ten equal amounts. After the resulting mixture had been stirred for 3 days at room temperature, water (5 c.c.) was added and the mixture heated at 100° for 0·5 hr. The methylated product was isolated by extraction with chloroform (10 × 5 c.c.), and the syrup (27 mg.) was obtained by concentrating the dried extract and then submitted to a Purdie methylation. The syrup (22 mg.) was hydrolysed with 2N-sulphuric acid (1 c.c.) at 100° for 3 hr. Paper chromatography showed two components (equal amounts) with the R_F values of a tetra- and a tri-*O*-methylhexose respectively. Paper ionophoresis [8] of the hydrolysate in borate buffer of pH 10 showed the absence of both 3 : 4 : 6-tri-*O*-methylglucose and 3 : 4 : 6-tri-*O*-methylmannose.

Note: All the above work was carried out on the batch of polysaccharide produced by the Oxford University Physical Chemistry Laboratory strain of *Aerobacter aerogenes*. The methylation studies described below were carried out on the polysaccharide obtained from the morphologically identical N.C.T.C. 418 strain.

Methylation of Acidic Polysaccharide.—The polysaccharide (3·4 g.) was treated with sodium and methyl iodide in liquid ammonia at −70° according to Freudenberg and Boppel's method.[34] After four additions of the methylating reagents (reaction times: sodium 4 hr.; methyl iodide, 1 hr.) had been made, the ammonia was allowed to evaporate, with exclusion of moisture, the last traces being removed *in vacuo* at 90°. After dialysis, the freeze-dried product (3·4 g.) had OMe, 26·4%. Two repetitions of the methylation procedure gave products 2·4 g. and 1·79 g. which had OMe, 30·1% and OMe, 34·5% respectively. The crude methyl ether obtained after a final remethylation (1·35 g.) was dissolved in dry chloroform (300 c.c.) and light petroleum (40—60°; 275 c.c.) added. The insoluble material (0·075 g.) which was centrifuged off, suspended in water, and freeze-dried had OMe, 14·1%. The chloroform–petroleum-soluble fraction (1·28 g.) had OMe, 40%, and N, 1·13%. This methyl ether showed $[\alpha]_D^{16}$ +65·5° (*c* 0·35 in dry $CHCl_3$).

The infrared absorption spectra of the methylated acidic polysaccharide was measured as it was isolated and also in the free acid form. To obtain the latter, the methylated polysaccharide (10 mg.) was dissolved in methanol (0·5 c.c.) and treated with two drops of 5N-hydrochloric acid; the addition of methanol was necessary to bring the methyl ether into solution. The solution was dialysed for 3 days against running water and finally deionised with Amberlite IR-120 (2 c.c.).

Isolation of the Methyl Sugars from the Methylated Polysaccharide.—The methyl ether (1·25 g.) was refluxed with 4% methanolic hydrogen chloride (50 c.c.) for 6 hr. The solution was neutralised with silver carbonate, filtered, and evaporated *in vacuo* to a syrup. This syrup was

[34] Freudenberg and Boppel, *Ber.*, 1938, **71**, 2505.

XUM

hydrolysed with 2N-sulphuric acid (25 c.c.) for 3 hr. at 100°. The hydrolysate was neutralised with barium carbonate, filtered, and stirred with Deacidite FF (micro-bead; carbonate form) for 24 hr. The slurry was then poured into a column and washed with water (700 c.c.) to elute neutral methyl sugars (0·78 g.) and with N-ammonium carbonate (500 c.c.) to elute the methylated uronic acid fraction (0·056 g.). The latter was recovered by removing most of the ammonium carbonate by sublimation *in vacuo* at 65—70° and the remainder by pouring the solution down a column of Amberlite IR-120 (10 ml.).

Methylated uronic acid fraction. This fraction was separated on a Whatman No. 1 paper (46 × 57 cm.) irrigated with the butanol–acetic acid solvent and the strip bearing the component having an R_F value and staining properties identical with 2 : 3 : 4-tri-*O*-methylglucuronic acid eluted and concentrated (yield 18·4 mg.). On reduction of its methyl ester methyl glycoside with lithium aluminium hydride in ether (as above) and hydrolysis of the resulting methyl glycoside two components were detected on a paper chromatogram irrigated with butan-1-ol–ethanol–water (5 : 1 : 4). The two components were eluted. The faster-moving component had an R_F value and infrared spectrum identical with those of 2 : 3 : 4-tri-*O*-methyl-D-glucose. The slower-moving component had an R_F value and an M_G value (0·09) identical with those of the main di-*O*-methylhexose detected in the neutral sugar fraction (for characterisation see below). Examination of a hydrolysate (2N-sulphuric acid for 5 hr. at 100°) of the methylated uronic fraction (1 mg.) before reduction showed the same di-*O*-methylhexose together with 2 : 3 : 4-tri-*O*-methylglucuronic acid.

Neutral methyl sugars. The mixture of neutral methyl sugars (0·78 g.) was separated on 12 sheets of Whatman No. 3 MM paper (30 × 60 cm.) irrigated with butan-1-ol–ethanol–water (5 : 1 : 4). The three bands obtained on each paper corresponded to the tetra-, tri-, and di-*O*-methylhexose fractions respectively. A test hydrolysis on all of these showed that the tetra-*O*-methylhexose fraction only was contaminated with methyltrimethylglycoside. After rehydrolysis of this fraction with 2N-sulphuric acid (6 c.c.) for 6 hr. at 100° the components were separated again on paper as above. The weights of the fractions finally isolated together with that of the purified tri-*O*-methyluronic acid corresponded to the following molecular composition: di-*O*-methylhexose fraction, 5·1%; tri-*O*-methylhexose fraction, 90%; tetra-*O*-methylhexose fraction, 2·3%; tri-*O*-methylhexuronic acid, 2·6%.

Tetra-O-*methylhexose fraction.* This fraction showed $[\alpha]_D^{20}$ +66° approx. (*c* 0·18 in H_2O) and on paper chromatography showed a single well-defined component with an R_F value identical with that of 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose. Its infrared spectrum was also identical with that of 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose eluted from the paper under comparable conditions

Tri-O-*methylhexose fraction.* The fraction had $[\alpha]_D^{20}$ +69° (*c* 0·39 in MeOH) (Found: OMe, 42·1. Calc. for a tri-*O*-methylhexose: OMe, 41·9%). Paper ionophoresis [8] in borate buffer of pH 10 showed the absence of both 3 : 4 : 6-tri-*O*-methylglucose and 3 : 4 : 6-tri-*O*-methylmannose. A portion (30 mg.) of the tri-*O*-methylhexose fraction was treated with aqueous sodium borohydride (30 mg. in 2·5 c.c.) at room temperature for 4 hr. The excess of sodium borohydride was destroyed with glacial acetic acid, and the solution deionised on an Amberlite IR-120 and IR-4B mixed-bed resin. The effluent was concentrated to a syrup (0·0178 g.) and oxidised with periodate under the conditions described above. The tri-*O*-methylhexitol fraction consumed 0·93 mole (6 hr.), 0·96 mole (24 hr.) of periodate per mole but produced no formic acid.

Paper chromatography of the tri-*O*-methylhexose fraction in butan-1-ol–ethanol–water (5 : 1 : 4) disclosed at least two components. Although these showed little relative separation a portion of the tri-*O*-methylhexose fraction was fractionated by paper chromatography into A (slower components) and B (faster components). A showed $[\alpha]_D^{20}$ +36·4° (*c* 0·714 in H_2O) and on demethylation [27] gave, *inter alia*, both glucose and mannose. Part of A (30 mg.) was refluxed with aniline (30 mg.) in ethanol (1 c.c.) for 3 hr. and gave 2 : 4 : 6-tri-*O*-methyl-*N*-phenyl-D-glucosylamine (2 mg.), m. p. and mixed m. p. 161°. B showed $[\alpha]_D^{20}$ +45° (*c* 0·756 in H_2O) and on demethylation [27] gave, *inter alia*, both glucose and mannose, the latter in smaller amount. B was kept in 2% methanolic hydrogen chloride at room temperature and the falling rotation observed until constant. It showed $[\alpha]_D^{22}$ +50·7° (10 min.) ⟶ +7·2° (24 hr.; *c* 0·552). The solution was neutralised with silver carbonate, filtered, and concentrated. A paper chromatogram, bearing spots of equal amounts of B before and after treatment with methanolic hydrogen chloride, was irrigated with butan-1-ol–ethanol–water (5 : 1 : 4). Spraying

with aniline hydrogen phthalate showed the disappearance of the region corresponding to 2 : 3 : 6-tri-*O*-methyl-D-glucose. After spraying with dilute hydrochloric acid and heating, a faster-moving component, presumably the methyl glycoside of this methyl ether, appeared.

Di-O-methylhexose fraction. The fraction had $[\alpha]_D^{20}$ +9·1° (*c* 0·44 in H_2O) and on paper ionophoresis [8] in borate buffer of pH 10 showed the presence of one major component (M_G 0·092) and traces of two other components having M_G values identical with those of 2 : 3-di-*O*-methyl-glucose (or -mannose) and 2 : 4-di-*O*-methyl-glucose (or -mannose). Reference di-*O*-methylglucoses had M_G 0·0 (2 : 4-), 0·135 (2 : 3-), 0·28 (3 : 4-), 0·546 (3 : 6-), 0·185 (4 : 6-) while reference di-*O*-methylmannoses had M_G 0·136 (2 : 3-), 0·514 (3 : 4-), 0·44 (4 : 6-). On demethylation [27] the di-*O*-methylhexose fraction gave, *inter alia*, mannose and glucose. When reduced with sodium borohydride, under the conditions described for the tri-*O*-methylhexose fraction, the resulting di-*O*-methylhexitol fraction consumed 0·74 mole (6 hr.), 0·9 mole (24 hr.) of periodate and produced 1·72 moles (6 hr.), 1·9 moles (24 hr.) of formic acid per mole. No formaldehyde was produced.

The authors are indebted to Dr. A. S. Jones for valuable advice, to Professor M. Heidelberger for determining the immunological specificity of the polysaccharide, and to Dr. Kelly of the Antibiotics Research Station, Clevedon, for providing large-scale facilities for its production. One of them (I. R. S.) thanks the British Council for a scholarship under the Colombo Plan.

CHEMISTRY DEPARTMENT, THE UNIVERSITY,
EDGBASTON, BIRMINGHAM, 15.

[*Received, February 7th*, 1958.]

---

473. *Flavan Derivatives. Part I. The Absolute Configuration of (+)-Dihydroquercetin.*

By J. W. CLARK-LEWIS and W. KORYTNYK.

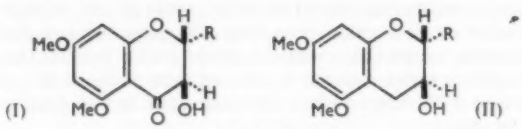
The *trans*-configuration is proved for (+)-dihydroquercetin and its racemate, and the absolute configurations of the two asymmetric centres in (+)-dihydroquercetin are shown to be identical with those in (+)-catechin. (+)-Catechin tetramethyl ether 3-toluene-*p*-sulphonate has been re-investigated; when heated with ethanolic potassium acetate it suffered a Wagner–Meerwein rearrangement to (+)-2-ethoxy-5 : 7 : 3′ : 4′-tetramethoxy*iso*-flavan.

CONSIDERABLE interest in the stereochemical relations of reduced flavan or dihydro-2-phenylbenzopyran derivatives is apparent from recent communications concerning catechins,[1–8] *leuco*anthocyanidins,[4, 7, 9–12] and dihydroflavonols.[4, 7, 13–15] Interconversions of these three classes of compound presumably occur in plant tissues, although details of

[1] King, Clark-Lewis, and Forbes, *J.*, 1955, 2948.
[2] Clark-Lewis, *Chem. and Ind.*, 1955, 1218.
[3] Roberts, *ibid.*, 1955, 631, 1551; 1956, 737.
[4] Whalley, "Chemistry of Vegetable Tannins," Soc. Leather Trades' Chemists, Croydon, 1956, p. 151.
[5] Freudenberg, *Sci. Proc. Roy. Dublin Soc.*, 1956, **27**, 153.
[6] Birch, Clark-Lewis, and Robertson, *J.*, 1957, 3586.
[7] Clark-Lewis, "Stereochemistry of Catechins and Related Flavan Derivatives," Symposium on Heterocyclic Chemistry, Canberra, September 1957, Chem. Soc. Spec. Publ., in the press.
[8] Hardegger, Gempeler, and Züst, *Helv. Chim. Acta*, 1957, **40**, 1819.
[9] King and Clark-Lewis, *J.*, 1955, 3384.
[10] King, *Sci. Proc. Roy. Dublin Soc.*, 1956, **27**, 87.
[11] Kulkarni and Joshi, *Chem. and Ind.*, 1954, 1456; 1956, 124.
[12] Bognár and Rákosi, *ibid.*, 1956, 188.
[13] Mahesh and Seshadri, *Proc. Indian Acad. Sci.*, 1955, **41**, *A*, 210.
[14] Gowan, Philbin, and Wheeler, "Chemistry of Vegetable Tannins," Soc. Leather Trades' Chemists, Croydon, 1956, p. 133.
[15] Kulkarni and Joshi, *J. Indian Chem. Soc.*, 1957, **34**, 217.

XUM

such transformations remain obscure.[16] In the laboratory both dihydroflavonols and flavan-3 : 4-diols can be converted into catechins by removal of the oxygen function from the 4-position, and the catechins [6,7] are therefore key compounds in stereochemical correlations of flavan derivatives. Correlation has shown that (+)-dihydroquercetin is stereochemically identical with (+)-catechin; this confirms the assignment [4,13] of the dihydroflavonol to the *trans*-series (2H : 3H *trans*) and establishes the absolute configurations of both asymmetric centres.



R = 3:4-$(MeO)_2C_6H_3$.

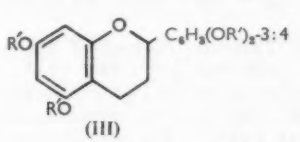
(+)-Dihydroquercetin (taxifolin) was first isolated [17] from the heartwood of Douglas fir and has since been obtained from the bark [18] and from other sources.[14] Methylation of (+)-dihydroquercetin by the acetone–potassium carbonate method already described for the (±)-compound [19] gave (+)-dihydroquercetin 5 : 7 : 3′ : 4′-tetramethyl ether (I), $[\alpha]_D$ −23·4°, which was converted by hydrogenation over Adams platinic oxide catalyst into (+)-catechin tetramethyl ether (II), $[\alpha]_D$ −9·8° (in $CHCl_3$), as noted in a preliminary communication.[20] The identity of the product with an authentic specimen prepared by methylation of (+)-catechin was established by mixed m. p. determination and by comparison of infrared absorption spectra (Nujol mulls and CCl_4 solutions). The absolute configurations of (+)-dihydroquercetin and (+)-catechin tetramethyl ethers are therefore identical, as shown in the formulæ (I) and (II), and the parent compounds may be described respectively as (2*R* : 3*R*)-5 : 7 : 3′ : 4′-tetrahydroxy-4-oxoflavan-3-ol and (2*R* : 3*S*)-5 : 7 : 3′ : 4′-tetrahydroxyflavan-3-ol according to Cahn, Ingold, and Prelog's method for specifying absolute configurations.[21]

After crystallisation of (+)-catechin tetramethyl ether (24%) the mother-liquors were evaporated and acetylation of the residue gave (±)-catechin tetramethyl ether 3-acetate (*ca.* 14%). Isolation of the (±)-catechin derivative indicated that the (+)-dihydroquercetin tetramethyl ether was optically impure. Recrystallisation of the latter from ethanol resulted in diminution of its specific rotation, but crystallisation of the 3-acetate from ethanol gave needles of (±)-dihydroquercetin tetramethyl ether 3-acetate and heavier rhombic crystals of the (+)-acetate, which was obtained with $[\alpha]_D$ +33·4° after several crystallisations. Shortage of material prevented completion of this purification process and there was insufficient for hydrolysis, so that the optical purities of the (+)-dihydroquercetin tetramethyl ether and its 3-acetate are not known. (+)-Dihydroquercetin and (+)-catechin show parallel changes in rotation on methylation and acetylation (see Table).

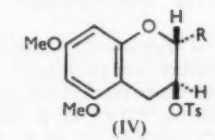
Compound	Specific rotation of (+)-catechin derivative	Specific rotation of (+)-dihydroquercetin derivative
Free phenol	$[\alpha]_{Hg}$ 0° in EtOH [22]	$[\alpha]_D$ +13° in EtOH [17]
	$[\alpha]_{Hg}$ +17° in 50% acetone [22]	$[\alpha]_D$ +46° in 50% acetone [17]
Tetramethyl ether	$[\alpha]_{Hg}$ −13·4° in $C_2H_2Cl_4$ [22]	—
	$[\alpha]_D$ −13·4° in $C_2H_2Cl_4$ [6]	—
	$[\alpha]_D$ −11·4° in $CHCl_3$	$[\alpha]_D$ −23·4° in $CHCl_3$
Tetramethyl ether 3-acetate	$[\alpha]_{Hg}$ +6·8° in $C_2H_2Cl_4$ [22]	$[\alpha]_D$ +33·4° in $CHCl_3$

[16] Swain and Bate-Smith, "Chemistry of Vegetable Tannins," Soc. Leather Trades' Chemists, Croydon, 1956, p. 109; Hillis, *ibid.*, p. 121; Bate-Smith, *ibid.*, p. 143; Hillis, *Austral. J. Biol. Sci.*, 1956, **9**, 263.
[17] Pew, *J. Amer. Chem. Soc.*, 1948, **70**, 3031.
[18] Kurth and Chan, *J. Amer. Leather Chemists' Assoc.*, 1953, **48**, 20; cf. ref. 19.
[19] Hergert, Coad, and Logan, *J. Org. Chem.*, 1956, **21**, 304.
[20] Clark-Lewis and Korytnyk, *Chem. and Ind.*, 1957, 1418.
[21] Cahn, Ingold, and Prelog, *Experientia*, 1956, **12**, 81.
[22] Freudenberg and Purrmann, *Annalen*, 1924, **437**, 274.

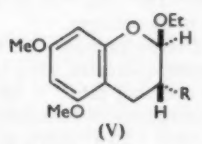
(+)-Dihydroflavonols theoretically could exist in *cis*- and *trans*-forms and yield *cis*- and *trans*-racemates, but racemisation of naturally occurring (+)-dihydroquercetin with acid [17] or with bases [23] yields a single racemate which is identical [23] with that obtained from quercetin by reduction with sodium dithionite.[17,24] This product is the *trans*-racemate, as shown by conversion of its tetramethyl ether [prepared from acid-racemised [17] (±)-dihydroquercetin] into (±)-catechin tetramethyl ether, and supported by the identity in infrared absorption of solutions of (+)- and (±)-dihydroquercetin tetramethyl ether. Distylin (from *Distylium racemosum*) is a naturally occurring form of *trans*-(±)-dihydroquercetin, as shown by its identity [25] with racemic Douglas-fir flavanone.



(III)



(IV)



(V)

R = 3 : 4-(MeO)$_2$C$_6$H$_3$. Ts = *p*-C$_6$H$_4$Me·SO$_2$.

The central importance of catechins for elucidation of the stereochemistry of flavan derivatives prompted investigation of two possible (but unsuccessful) methods for confirming the established [6] configurations. Direct comparison of the configurations at the 2-positions of (+)-catechin and (−)-*epi*catechin would be achieved by removal of the oxygen function at the 3-position to yield the flavan (III; R′ = H or Me); (+)-catechin tetramethyl ether 3-toluene-*p*-sulphonate (IV) was accordingly treated with lithium aluminium hydride in the hope that alkyl–oxygen fission would ensue, but the toluene-*p*-sulphonate was unaffected. (+)-Catechin tetramethyl ether 3-toluene-*p*-sulphonate was found to be dimorphic (m. p.s 86—88° and 115—116°) and to have $[\alpha]_D$ +87·7° instead of the reported value (+22·7°),[26] which is apparently a miscalculation for 91·8°. Replacement of the toluene-*p*-sulphonyloxy-group by acetoxyl was attempted by heating the (+)-catechin derivative (IV) with alcoholic potassium acetate, as the desired replacement with Walden inversion would not only have confirmed the relative configurations of (+)-catechin and (−)-*epi*catechin but would also have provided a convenient source of the less easily accessible (−)-*epi*catechin derivatives. Reaction was incomplete in boiling solution and under more vigorous conditions (sealed tube) the product was (+)-2-ethoxy-5 : 7 : 3′ : 4′-tetramethoxy*iso*flavan (V), which previously had been obtained from the 2-chloro*iso*flavan resulting from the action of phosphorus pentachloride on (+)-catechin tetramethyl ether.[27-30] These rearrangements are of particular interest because they proceed with retention of optical activity, and it is clear that inversion occurs at the 3-position as a result of neighbouring-group participation (cf. Whalley [4]). The configuration at the 2-position is less certain, but the 2-ethoxy*iso*flavan is tentatively regarded as the *trans*-compound (V) formed by inversion at both centres, for which there are analogies in other cases of Wagner–Meerwein transformation.[31] The confirmation of configurations which we hoped to achieve with (+)-catechin tetramethyl ether toluene-*p*-sulphonate has since been provided by exhaustive ozonisation of (+)-catechin,[8] a method completely independent of that originally employed.[6]

[23] Kurth, Hergert, and Ross, *J. Amer. Chem. Soc.*, 1955, **77**, 1621.
[24] Geissman and Lischner, *ibid.*, 1952, **74**, 3001.
[25] Kondo, *J. Fac. Agric. Kyushu Univ.*, 1951, **10**, 79, 101; *Chem. Abs.*, 1953, **47**, 4602.
[26] Freudenberg, Orthner, and Fikentscher, *Annalen*, 1924, **436**, 286.
[27] Drumm, *Proc. Roy. Irish Acad.*, 1923—1924, **36***B*, 41.
[28] Drumm, Carolan, and Ryan, *ibid.*, 1929, **39***B*, 114.
[29] Freudenberg, Carrara, and Cohn, *Annalen*, 1926, **446**, 87.
[30] Baker, *J.*, 1929, 1593.
[31] Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 510; Cram in Newman's "Steric Effects in Organic Chemistry," Wiley, New York, 1956, p. 255.

XUM

Experimental

(±)-*Dihydroquercetin* 5 : 7 : 3′ : 4′-*tetramethyl ether*, m. p. 169—170°, was prepared from (±)-dihydroquercetin (acid-racemised [17]) as described by Hergert, Coad, and Logan [19] (Found: C, 63·3; H, 5·68. Calc. for $C_{19}H_{20}O_7$: C, 63·3; H, 5·6%); the infrared absorption of the (±)-compound (in CCl_4) was indistinguishable from that of the optically active isomer described below, with OH and carbonyl absorption at 2·85 and 5·92 μ. A solution of the methyl ether (0·45 g.) in pyridine (4 c.c.) and acetic anhydride (4 c.c.) was kept at room temperature for 14 hr. and was then poured into water; the precipitated oil crystallised rapidly and recrystallisation from ethanol gave (±)-dihydroquercetin tetramethyl ether 3-acetate (0·43 g.) as needles, m. p. 184—185° (lit.,[19] m. p. 171—172°, from methanol, and [25] 186°), which had no observable rotation in chloroform.

(+)-*Dihydroquercetin* 5 : 7 : 3′ : 4′-*Tetramethyl Ether* (*Taxifolin Tetramethyl Ether*) (I).—(+)-Dihydroquercetin, after being dried over phosphoric oxide, had $[\alpha]_D^{18}$ +39·7° (2·5% in 50% aqueous acetone) (lit.,[17] +46°), and when methylated (5 g.) as for the (±)-compound [19] gave (+)-*dihydroquercetin tetramethyl ether* (*ca.* 3·0 g.), m. p. 165—168° after two crystallisations from ethanol, $[\alpha]_D^{16}$ −23·4° (2·3% in $CHCl_3$) (Found: C, 62·9; H, 5·75%). The optical purity of this product is unknown; recrystallisation of optically impure material from ethanol reduced the specific rotation; *e.g.*, material with $[\alpha]_D$ −20·3° had $[\alpha]_D$ −17·8° (1·2% in $CHCl_3$) after two crystallisations from ethanol. In a similar methylation partly racemised dihydroquercetin (9·25 g.), $[\alpha]_D^{18}$ +26·9° (2·8% in 50% aqueous acetone), gave the tetramethyl ether (5·32 g.) with $[\alpha]_D^{19}$ −9·9° (2·7% in $CHCl_3$). (+)-Dihydroquercetin tetramethyl ether (0·4255 g.), $[\alpha]_D^{18}$ −19·7° (2·4% in $CHCl_3$), was dissolved in acetic acid (10 c.c.) and the observed rotation (−0·29°) was unchanged after 15 days at room temperature (18—20°), $[\alpha]_D$ −6·8° (4·3% in AcOH).

(+)-*Dihydroquercetin Tetramethyl Ether 3-Acetate*.—A solution of (+)-dihydroquercetin tetramethyl ether (0·40 g.), $[\alpha]_D^{18}$ −19·7° (in $CHCl_3$), in pyridine (1 c.c.) and acetic anhydride (1 c.c.) was kept for 5 hr. and then added to water. Crystallisation of the precipitated solid from ethanol gave crude product (0·35 g.) in rhombic crystals, m. p. 164—165° after softening at 159°, $[\alpha]_D^{18}$ +17·9° (1·7% in $CHCl_3$). Recrystallisation from ethanol gave a mixture of fine needles and larger rhombic crystals which were separated mechanically (swirling and filtering): the needles (0·066 g.) consisted of (±)-dihydroquercetin tetramethyl ether 3-acetate, m. p. 182—183° alone and when mixed with authentic material. The heavier rhombic crystals (0·258 g.), m. p. *ca.* 165°, $[\alpha]_D^{15}$ +22·9° (1·8% in $CHCl_3$), after two recrystallisations from ethanol and separation from further needle crystals of (±)-acetate, gave the (+)-*acetate* in rhombic crystals, m. p. 162—163°, $[\alpha]_D^{18}$ +33·4° (2·1% in $CHCl_3$) (Found: C, 62·5; H, 5·48; Ac, 10·5. $C_{21}H_{22}O_8$ requires C, 62·7; H, 5·51; Ac, 10·7%). Insufficient material remained for further recrystallisation, but the specific rotation (33·4°) was not exceeded in two subsequent experiments; the optical purity of this (+)-acetate is unknown.

(±)-*Catechin* 5 : 7 : 3′ : 4′-*Tetramethyl Ether from* (±)-*Dihydroquercetin Tetramethyl Ether*.—A suspension of platinic oxide (0·1 g.) in acetic acid was reduced by hydrogen for 3 hr. before introduction of a suspension of (±)-dihydroquercetin tetramethyl ether (1 g.) in acetic acid (*ca.* 20 c.c.). The mixture was shaken with hydrogen at room temperature and pressure until hydrogenation appeared to be complete (17 hr.) and the catalyst was removed at the centrifuge. Evaporation of the supernatant solution left a crystalline residue which, after recrystallisation from ethanol, gave a product (0·56 g.), m. p. 154—164°. This was acetylated with acetic anhydride–pyridine (1 : 1) for 14 hr. at room temperature; the crystalline product obtained by adding the acetylation mixture to water consisted of (±)-catechin tetramethyl ether 3-acetate which crystallised from ethanol in needles (0·28 g.), m. p. 134—135° raised to 135—136° by recrystallisation (lit.,[22] m. p. 134—135°) (Found: C, 64·9; H, 6·27; Ac, 9·8. Calc. for $C_{21}H_{24}O_7$: C, 64·9; H, 6·24; Ac, 11·1%). The infrared absorption (in CCl_4) of the (±)-acetate was indistinguishable from that of (+)-catechin tetramethyl ether 3-acetate but differed from that of (−)-*epi*catechin tetramethyl ether 3-acetate.

(+)-*Catechin* 5 : 7 : 3′ : 4′-*Tetramethyl Ether* (II) *from* (+)-*Dihydroquercetin Tetramethyl Ether* (I).—(+)-Dihydroquercetin tetramethyl ether (1 g.), $[\alpha]_D^{16}$ −23·4° (in $CHCl_3$), was hydrogenated over Adams catalyst as already described for the (±)-compound. Removal of the catalyst and evaporation of the solvent left an oil, $[\alpha]_D^{18}$ −5·6° (1·4% in $CHCl_3$), with infrared absorption (CCl_4 solution) closely similar to that of (+)-catechin tetramethyl ether except

for a band at 5·8 μ which was probably due to traces of acetic acid or an acetate as dihydroquercetin tetramethyl ether carbonyl absorption occurred at 5·92 μ. The oil crystallised from aqueous ethanol in needles (0·23 g., 24%), m. p. 138—140° raised by several crystallisations from aqueous ethanol to m. p. 140—141°, $[\alpha]_D^{18}$ −9·8° (1·6% in $CHCl_3$), which did not depress the m. p. of authentic (+)-catechin 5 : 7 : 3′ : 4′-tetramethyl ether, m. p. 141—142°, $[\alpha]_D^{23}$ −11·4° (4·5% in $CHCl_3$). The infrared absorption (CCl_4 and Nujol mull) of the product was indistinguishable from that of authentic (+)-catechin tetramethyl ether, but differed from that of (−)-*epi*catechin tetramethyl ether (in CCl_4).

The filtrate from the first crop of crystals (0·23 g.) was evaporated under reduced pressure and the residue, on acetylation with acetic anhydride and pyridine at room temperature, gave (±)-catechin tetramethyl ether 3-acetate (*ca.* 0·15 g.), m. p. and mixed m. p. 135—136°. Ester carbonyl absorption occurred at 5·72 μ (CCl_4 solution).

(+)-*Catechin* 5 : 7 : 3′ : 4′-*Tetramethyl Ether* (II) *from* (+)-*Catechin*.—A mixture of partly racemised (+)-catechin (11 g.), $[\alpha]_D^{24}$ +9·3° (0·9% in 50% aqueous acetone) (lit.,[32] $[\alpha]_{Hg}$ +17·1°), anhydrous potassium carbonate (25 g.), and dry acetone was heated to the b. p. before addition of dimethyl sulphate (13·2 c.c.) in three portions, and gentle boiling was maintained for 4 hr. (total). The suspension was filtered, the residue was washed with acetone, and the combined acetone filtrates were treated with a few drops of aqueous ammonia and evaporated on a steam-bath. Recrystallisation of the residue from methanol gave (+)-catechin tetramethyl ether (8·7 g.) in needles, m. p. 141—142°, $[\alpha]_D^{25}$ −11·2° (4·5% in $CHCl_3$), raised by recrystallisation to m. p. 142—143°, $[\alpha]_D^{23}$ −11·4° (4·5% in $CHCl_3$) and then to m. p. 143—144°, $[\alpha]_D^{22}$ −13·3° (4·3% in $C_2H_2Cl_4$) {lit.,[32] m. p. 143—144°, $[\alpha]_{Hg}$ −13·4° (3% in $C_2H_2Cl_4$)} (Found: C, 66·1; H, 6·25. Calc. for $C_{19}H_{22}O_6$: C, 65·9; H, 6·40%). The acetate [32] melted at 94—95°.

(+)-*Catechin Tetramethyl Ether* 3-*Toluene*-p-*sulphonate* (IV).—This was prepared from the foregoing methyl ether by Freudenberg, Orthner, and Fikentscher's method [26] and after three crystallisations from methanol had m. p. 86—88° and $[\alpha]_D^{21}$ +87·7° (6·1% in $C_2H_2Cl_4$) {lit.,[26] m. p. 86—87°, $[\alpha]_D^{14}$ +22·7° or, after recalculation, +91·8° (in $C_2H_2Cl_4$)}. The toluene-*p*-sulphonate crystallised from ethanol in plates, m. p. 114—116° raised to 115—116° by recrystallisation (Found: C, 62·4; H, 5·71. Calc. for $C_{26}H_{28}O_8S$: C, 62·4; H, 5·64%); crystallisation from methanol then gave needles, m. p. 86—88°, once more, and a mixture of the two sintered slightly at the lower temperature and melted at 110°. The toluene-*p*-sulphonate was recovered after being treated with lithium aluminium hydride under the conditions applied [33] to codeine toluene-*p*-sulphonate, and similar results were obtained with anhydrous dioxan as solvent in place of tetrahydrofuran.

Rearrangement of (+)-*Catechin Tetramethyl Ether* 3-*Toluene*-p-*sulphonate with Ethanolic Potassium Acetate*.—A solution of (+)-catechin tetramethyl ether 3-toluene-*p*-sulphonate (1 g.) and freshly fused potassium acetate in magnesium-dried ethanol (15 c.c.) was heated in a sealed tube at 135° for 48 hr. The cold solution was filtered from potassium toluene-*p*-sulphonate (0·367 g., 94·5%), then evaporation left a dark brown oil (0·67 g.), $[\alpha]_D^{18}$ +16·8° (0·8% in $C_2H_2Cl_4$), which was dissolved in a little methanol. Crystallisation gave (+)-2-ethoxy-5 : 7 : 3′ : 4′-tetramethoxy*iso*flavan (0·143 g.) in needles, m. p. 122—123° raised by two crystallisations to m. p. 123—124°, $[\alpha]_D^{20}$ +113·2° (1·1% in $C_2H_2Cl_4$) (Found: C, 67·6; H, 7·01; OAlk calc. as OMe, 39·8; *C*-Me, 3·9. Calc. for $C_{21}H_{26}O_6$: C, 67·4; H, 7·00; OMe, 41·4; *C*-Me, 4%); Drumm [27] reports m. p. 123°, and Drumm, Carolan, and Ryan [28] record $[\alpha]_D^{16}$ +119° (3·0% in $C_2H_2Cl_4$). The m. p. of the product was not depressed by admixture with the authentic specimen described below. A small quantity of unidentified material was obtained from the mother-liquors in needles (*ca.* 0·03 g.), m. p. 100—102°, $[\alpha]_D^{20}$ +14·9° (0·6% in $C_2H_2Cl_4$).

With methanolic potassium acetate the toluene-*p*-sulphonate (1 g.) similarly gave a brown oil (0·626 g.), $[\alpha]_D$ +34·3° (0·9% in $C_2H_2Cl_4$), from which no crystalline compound was isolated. With ethanolic potassium acetate under milder conditions (boiling for 11 hr.) conversion was incomplete and the toluene-*p*-sulphonate (20%) was recovered with $[\alpha]_D^{23}$ +84·4° ($C_2H_2Cl_4$).

(+)-2-*Ethoxy*-5 : 7 : 3′ : 4′-*tetramethoxy*iso*flavan* (V).—The intermediate 2-chloro*iso*flavan was not obtained crystalline when prepared according to Drumm's directions [27] (see also Baker [30]) and in subsequent work carbon disulphide was replaced by benzene. Phosphorus pentachloride (0·7 g.) was added to (+)-catechin 5 : 7 : 3′ : 4′-tetramethyl ether (1 g.) in dry (Na) benzene (20 c.c.) and the flask was immediately closed with a calcium chloride guard tube

[32] Freudenberg, Böhme, and Purrmann, *Ber.*, 1922, **55**, 1746.
[33] Rapoport and Bonner, *J. Amer. Chem. Soc.*, 1951, **73**, 2872.

XUM

and shaken. When the reaction appeared complete (5 min.) the reddish solution was stirred with aqueous sodium carbonate, and the organic layer was separated and washed twice with aqueous sodium carbonate, and then once with water. Benzene was removed by distillation under reduced pressure and the oily residue was heated under reflux with dry ethanol (10 c.c.) for 30 min. and then allowed to cool. (+)-2-Ethoxy-5 : 7 : 3′ : 4′-tetramethoxy*iso*flavan crystallised in needles (0·7 g.), $[\alpha]_D^{24}$ +119° (0·5% in $C_2H_2Cl_4$), m. p. 122—123° alone and when mixed with the compound prepared from (+)-catechin tetramethyl ether 3-toluene-*p*-sulphonate as already described.

2-Ethoxy-5 : 7 : 3′ : 4′-tetramethoxy*iso*flavan (0·5 g.), $[\alpha]_D^{24}$ +119°, was recovered after being heated in a sealed tube with potassium acetate (0·5 g.) and dry ethanol (8 c.c.) at 135° for 48 hr. The solution was diluted with water and extracted with chloroform; evaporation of the chloroform left a crystalline residue (0·5 g.), which was too dark for polarimetry. Recrystallisation of the residue from ethanol gave needles (0·389 g.), $[\alpha]_D^{24}$ +117° (0·9% in $C_2H_2Cl_4$), m. p. 123—124° alone and when mixed with the starting material.

The authors thank Dr. H. J. Rodda for infrared measurements, and Dr. Herbert L. Hergert and the Oregon Forest Products Laboratory for gifts of (+)-catechin and (+)- and (±)-dihydroquercetin, and Professor A. J. Birch and Mr. A. V. Robertson for specimens of (−)-*epi*catechin 5 : 7 : 3′ : 4′-tetramethyl ether and its 3-acetate. They also thank the Commonwealth Scientific and Industrial Research Organisation for an Australian studentship (to W. K.). Microanalyses were performed in the C.S.I.R.O. Microanalytical Laboratory, Melbourne.

UNIVERSITY OF ADELAIDE, SOUTH AUSTRALIA. [*Received, February 10th*, 1958.]

---

474. *Peroxides of Elements other than Carbon. Part II.*[1] *The Formation of Boron Peroxides by Nucleophilic Substitution.*

By ALWYN G. DAVIES and R. B. MOODIE.

Boron trichloride with *tert.*- and with *n*-butyl hydroperoxide forms the corresponding tri(alkylperoxy)boron compounds, $(RO{\cdot}O)_3B$. Tetra-acetyl diborate gives the di(alkylperoxy)boron hydroxide $(RO{\cdot}O)_2B{\cdot}OH$; *o*-nitrophenyl dichloroboronite $Cl_2B{\cdot}OAr$ and di-(*o*-nitrophenyl) chloroboronate $ClB(OAr)_2$ yield the alkylperoxy-aryloxy-compounds $(RO{\cdot}O)_2B{\cdot}OAr$ and $RO{\cdot}OB(OAr)_2$ respectively.

Alkylboronic acids $R{\cdot}B(OH)_2$ and their derivatives reduce alkyl hydroperoxides and liberate the alcohol (or phenol) ROH. This reaction, carried out with an ^{18}O-labelled boronic acid, and with an optically active alkyl hydroperoxide, proceeds consistently with a mechanism involving nucleophilic migration of the group R from boron to oxygen in the framework R–B–O–O–R′.

IN Part I[1] we described silicon peroxides which were prepared by the nucleophilic attack of peroxides on, in particular, chlorosilanes. This paper reports the organoperoxyboron compounds which are prepared by analogous reactions.

Derivatives of Boric Acid.—Boron trichloride with *tert.*- and with *n*-butyl hydroperoxide gives the corresponding tri(alkylperoxy)boron compounds in good yield:

$$3RO{\cdot}OH + BCl_3 \longrightarrow (RO{\cdot}O)_3B + 3HCl$$

The products are colourless liquids, stable for some months at room temperature or for short periods at 100°, but initiating the slow polymerisation of styrene at 45°, presumably by O–O homolysis.

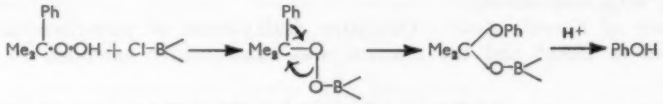
Both compounds reacted with water or ethanol rapidly and completely, liberating the corresponding hydroperoxide, and (cf. the peroxysilanes[1]) we were not able to prepare the pure organoperoxyboron compounds by treating boric acid or boric esters with hydroperoxides. Tri-(*tert.*-butylperoxy)boron, but not the *n*-butyl compound, when treated

[1] Part I, Buncel and Davies, *J.*, 1958, 1550.

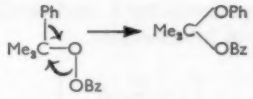
XUM

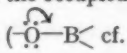
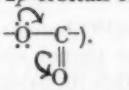
with ammonia, pyridine, or diethylamine in pentane, gave insoluble but rather unstable complexes.

The reaction between boron trichloride and 1-methyl-1-phenylethyl hydroperoxide was vigorous and phenol was isolated; similarly phenol was liberated exothermically from a mixture of *n*-propyl borate and the hydroperoxide at 70°. The reaction probably proceeds by O–O heterolysis accompanied by nucleophilic migration of the phenyl group from carbon to oxygen:



This is similar to the lability of 1-methyl-1-phenylethyl peroxybenzoate [2] and contrasts with the relative stability [1] of its silicon derivative $Ph{\cdot}CMe_2{\cdot}O{\cdot}O{\cdot}SiMe_3$.



Criegee [3] has shown that the lability of peresters RO·OX is related to the electron-attraction by the group −OX. In the boron derivatives this electron-attraction might arise by overlap of the occupied 2*p*-orbitals of the oxygen atom with the vacant 2*p*-orbitals of the boron atom ( cf. ).

The organoperoxy-derivatives of aluminium [4] and of cadmium [5] apparently exhibit a similar instability, which again may be associated with the presence of unfilled orbitals of low energy on the metal atom.

An attempt to prepare a triacylperoxyboron compound by reaction between boron trichloride and peroxyoctanoic acid apparently resulted in the oxidation of the chloride to molecular chlorine.

The reactivity of ethers towards boron trichloride, giving alkyl chloride and alkyl borate,[6] suggested that dialkyl peroxides might react similarly to form alkyl chlorides and alkylperoxy-compounds. The reaction between *tert.*-butyl peroxide and boron trichloride is vigorous at room temperature: *tert.*-butyl chloride and the corresponding olefin and hydrogen chloride are formed, together with an involatile boron compound with a low peroxidic content. The reaction is apparently analogous to that of ethers but does not constitute a useful preparative method.

Treatment of tetra-acetyl diborate $(AcO)_2BOB(OAc)_2$ with *tert.*-butyl hydroperoxide gave di-(*tert.*-butylperoxy)boron hydroxide $(Bu^tO{\cdot}O)_2B{\cdot}OH$. Whereas the tri(alkylperoxy)borons were unimolecular in boiling benzene, the dialkylperoxy-compound showed an anomalously high molecular weight indicating some molecular association. All three compounds absorbed strongly in the infrared region at about 1345 cm.$^{-1}$, which has been attributed to the B–O stretching frequency.[7]*

Many mixed alkoxides of silicon are known, and we isolated (*tert.*-butylperoxy)triethoxysilane on reaction of *tert.*-butyl hydroperoxide with triethoxychlorosilane.[1] On the

* This frequency is absent in the spectrum of tetra-acetyl diborate because the B–O bond multiplicity is lowered by intramolecular association between the boron atom and a carbonyl-oxygen atom; the case of the diethanolamine esters of boronic acids is similar.

[1] Hock and Kropf, *Chem. Ber.*, 1955, **88**, 1544.
[2] Criegee, *Annalen*, 1948, **560**, 127.
[4] Davies and Hall, unpublished work.
[5] Davies and Packer, unpublished work.
[6] Gerrard and Lappert, *J.*, 1952, 1486.
[7] Werner and O'Brien, *Austral. J. Chem.*, 1955, **8**, 355; 1956, **9**, 137.

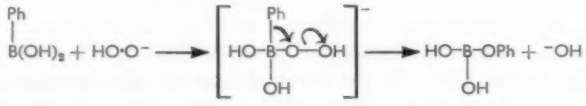
XUM

other hand, mixed alkoxides of boron readily disproportionate to the symmetrical compounds, and no simple examples have apparently yet been described. Mixed ethoxy-*o*-nitrophenoxyboron compounds, however, have recently been shown to be stable, probably because of intramolecular association between the nitro-group and boron atom.[8] Likewise the di-(*tert.*-butylperoxy)-*o*-nitrophenoxyboron and *tert.*-butylperoxydi-*o*-nitrophenoxyboron were isolated as red oils from the reaction of *tert.*-butyl hydroperoxide with *o*-nitrophenyl dichloroboronite $Cl_2B{\cdot}O{\cdot}C_6H_4{\cdot}NO_2$ and di-*o*-nitrophenyl chloroboronate $ClB(O{\cdot}C_6H_4{\cdot}NO_2)_2$ respectively.

Derivatives of Boronic Acids.—Oxidative dealkylation of phenylboronic acid was demonstrated in 1930,[9] and the reaction was subsequently extended to alkylboron compounds:

$$Ph{\cdot}B(OH)_2 + H_2O_2 \longrightarrow B(OH)_3 + PhOH$$

Kuivila and his co-workers [10] presented kinetic evidence that reaction of arylboronic acids with hydrogen peroxide proceeds by a nucleophilic shift of the aryl group from boron to oxygen in a four-covalent intermediate:



We have repeated this reaction with phenyl[^{18}O]boronic acid in [^{18}O]water containing isotopically normal hydrogen peroxide. The phenol which was formed was of normal isotopic composition, and must therefore derive its oxygen from the hydrogen peroxide, as is required by Kuivila's mechanism.

A similar reaction takes place when organoboron compounds are treated with alkyl hydroperoxides. When phenyl[^{18}O]boronic acid was treated with 1 : 2 : 3 : 4-tetrahydro-1-naphthyl hydroperoxide in [^{18}O]aqueous dioxan, isotopically normal 1 : 2 : 3 : 4-tetrahydro-1-naphthol was obtained. The reaction therefore appears to be analogous to that described by Kuivila

Confirmation of this mechanism was obtained by carrying out the reaction with optically active 1-phenylethyl hydroperoxide under anhydrous conditions. Active 1-phenylethanol was isolated such that $\alpha(Ph{\cdot}CHMe{\cdot}OH)/\alpha(Ph{\cdot}CHMe{\cdot}O_2H) = +0{\cdot}34$. We have shown previously that this value probably indicates complete configurational retention in the 1-phenylethyl group,[11] which is compatible with the mechanism proposed.

This type of rearrangement has prevented our preparing the peroxy-analogues of boronic acids $R{\cdot}B(O{\cdot}OR)_2$ or boronous acids $R_2BO{\cdot}OR$ by nucleophilic substitution. For example, hexylboron difluoride reacts vigorously with *tert.*-butyl hydroperoxide to give hexanol and *tert.*-butyl peroxide, the latter probably arising by acid-catalysed condensation of the hydroperoxide with *tert.*-butyl alcohol, or with itself: [1]

$$C_6H_{13}{\cdot}BF_2 + Bu^tO{\cdot}O^- \longrightarrow F_2B{\cdot}OC_6H_{13} + Bu^tO^-$$

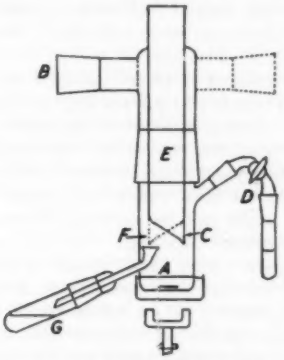
In contrast, alkylperoxysilanes containing the structure $R{-}\overset{|}{Si}{-}O{\cdot}OR$ are stable, and only the acylperoxysilanes $R{-}\overset{|}{Si}{\cdot}O{\cdot}O{\cdot}CO{\cdot}R$ rearranged.[1] We have, however, been able to isolate compounds containing the structure $R{-}\overset{|}{B}{-}O{\cdot}OR$ by autoxidation of boron alkyls [12] and to observe their rearrangement initiated by nucleophilic attack on boron.

[8] Colclough, Gerrard, and Lappert, *J.*, 1956, 3006.
[9] Ainsley and Challenger, *J.*, 1930, 2171.
[10] Kuivila and Armour, *J. Amer. Chem. Soc.*, 1957, **79**, 5659, and earlier papers.
[11] Davies and Feld, *J.*, 1956, 665.
[12] Abraham and Davies, *Chem. and Ind.*, 1957, 1622; Davies and Hare, unpublished work.

Experimental

General.—The usual precautions were taken against explosion; no trouble was encountered. Peroxidic oxygen was determined iodometrically and boron by titration as boric acid in the presence of mannitol.

To avoid the transference of easily hydrolysed and potentially hazardous material, the apparatus illustrated was used for preparing and purifying boron peroxides. When necessary, receivers were changed in a dry box. The use of the apparatus is described below.



Reaction between tert.-*Butyl Hydroperoxide and Boron Trichloride* —A solution of the hydroperoxide (8 g.) in an equal volume of pentane was placed in the apparatus at *A*, connected to the vacuum line at *B*. The cold-finger condenser, containing solid carbon dioxide–alcohol was arranged in position *C* for refluxing; boron trichloride (3·5 g.), cooled in the side-arm *D*, was then allowed to distil on warming into the hydroperoxide at *A*, cooled to 0°, and stirred magnetically.

The contents of *A* were allowed to warm to room temperature, hydrogen chloride being evolved. After 2 hours' stirring, the refrigerant in the cold-finger was removed, and the pentane and any residual hydroperoxide were taken off by successive reductions of pressure to 15 mm. and 1 mm. The condenser was then rotated about the axis of the B40 joint *E* to position *F* for distillation (broken lines), and the product distilled into the receiver *G* at 10^{-4} mm. from a bath at 40—70°.

The crude material, m. p. 12—15°, was recrystallised from pentane at −80° three times in the dry box, giving *tri*-(tert.-*butylperoxy*)*boron*, m. p. 15—18° [Found: C, 50·8; H, 9·4; B, 4·4; peroxidic O, 34·7%; *M* (ebullioscopically in benzene), 280. $C_{12}H_{27}O_6B$ requires C, 51·8; H, 9·8; B, 3·9; peroxidic O, 34·6%; *M*, 278].

Amine Complexes of Tri-(tert.-*butylperoxy*)*boron.*—When pyridine, diethylamine, or ammonia was added to a solution of the peroxy-compound in pentane, the amine complexes were precipitated. Filtration in a dry atmosphere gave a solid which dissociated and liquified at room temperature. The *pyridine complex* was the most stable (Found, on a freshly prepared sample: peroxidic O, 25·9. $C_5H_5N{\cdot}C_{12}H_{27}O_6B$ requires peroxidic O, 26·9%).

Reaction between n-*Butyl Hydroperoxide and Boron Trichloride.*—*n*-Butyl hydroperoxide, b. p. 42°/7·5 mm., n_D^{20} 1·4705, was prepared from *n*-butyl methanesulphonate in 20% yield by Williams and Mosher's method.[13]

The hydroperoxide (3·53 g.) in pentane (4 c.c.) was caused to react with boron trichloride (1·6 g.) by the above method, giving a good yield of *tri*-(n-*butylperoxy*)*boron*, b. p. 40—60° (bath)/10^{-3} mm., liquid at −80° (Found: C, 52·6; H, 9·75; B, 3·71; peroxidic O, 32·2%).

Reaction between 1-*Methyl*-1-*phenylethyl Hydroperoxide and Boron Trichloride.*—The reaction between the hydroperoxide (6·1 g.) in pentane (6 c.c.), and boron trichloride (2 g.), by the usual method was vigorous. Vacuum-sublimation of the brown liquid product gave phenol (2 g.) (tribromo-derivative, m. p. 93°).

[13] Williams and Mosher, *J. Amer. Chem. Soc.*, 1954, **76**, 2984.

XUM

Hydrolysis and Alcoholysis of Tri-(tert.-*butylperoxy*)*boron.*—A solution of the peroxy-compound in acetic acid containing sulphuric acid and triphenylmethanol, gave, by the usual method,[14] *tert.*-butyl triphenylmethyl peroxide, m. p. and mixed m. p. 72·5°.

Immediately after addition of dry ethanol (0·92 g.) to tri-(*tert.*-butylperoxy)boron (1·93 g.), no ethanol could be recovered at 30 mm. The product, presumably a mixture of ethyl borate and the hydroperoxide, distilled at 35—40°/16 mm.

Reaction between Hydroperoxides and Propyl Borate.—(i) In a preliminary experiment it was shown that propan-1-ol and *tert.*-butyl hydroperoxide can be separated by distillation at 60 mm. *tert.*-Butyl hydroperoxide (4·13 g.) and propyl borate (2·1 g.) were kept at 60°/60 mm. During 2 hr. a small volume of distillate was obtained (Found: peroxidic O, 20. Calc. for $C_4H_9O_2H$: peroxidic O, 35%). Unchanged hydroperoxide and alkyl borate were removed at 0·1 mm., leaving a residue (Found: peroxidic O, 21·5%).

(ii) No volatile material was obtained at 40 mm. when a mixture of 1-methyl-1-phenylethyl hydroperoxide (5·2 g.) and propyl borate (2·1 g.) was kept at room temperature for 3 hr. After a further 2 hr. at 70°/40 mm., a small amount of propanol was obtained; an exothermic reaction suddenly occurred and phenol was recovered from the product.

(iii) Pinane hydroperoxide (3·65 g.) and propyl borate (1·30 g.) were kept for 5 hr. at 80°/60 mm. Some propanol was collected. At 0·1 mm., much unchanged borate and hydroperoxide were recovered, leaving an oil which could not be distilled (Found: B, 2·2; peroxidic O, 14·7. Calc. for $C_{30}H_{51}O_6B$: B, 2·1; peroxidic O, 18·5%).

Reaction between Peroxyoctanoic Acid and Boron Trichloride.—Peroxyoctanoic acid (Found: peroxidic O, 20·1. Calc. for $C_8H_{16}O_3$: peroxidic O, 20·0%) was prepared by Swern and his co-workers' method [15] in 70% yield. When boron trichloride (0·88 g.) was distilled into the peroxy-acid (2·9 g.) in pentane at 0°, heat was evolved and the mixture became yellow. Volatile material carrying with it the yellow colour was removed at 15 mm. into a cold trap; the colour was lost when the liquid was warmed, and was apparently due to chlorine. At 10^{-2} mm. the pasty residue in the apparatus gave a sublimate of hexanoic acid on the cold-finger, leaving a residue of boric oxide.

Reaction between tert.-*Butyl Peroxide and Boron Trichloride.*—When a mixture of boron trichloride (2·35 g.) and *tert.*-butyl peroxide (7·8 g.) at −80° was allowed to warm to room temperature, a vigorous reaction took place. The volatile material contained hydrogen chloride (0·5 g.), olefin (0·3 g.), and *tert.*-butyl chloride (a trace, identified on the vapour-phase chromatogram [16]). Filtration of the residue gave boric acid, and hydrolysis of the mother-liquors liberated the hydroperoxide (0·2 g.).

Reaction between tert.-*Butyl Hydroperoxide and Tetra-acetyl Diborate.*—Tetra-acetyl diborate (Found: B, 7·75%; acid equiv., 46·0. Calc. for $C_8H_{12}O_9B_2$: B, 7·91%; acid equiv., 45·6) was prepared by reaction of boric acid with acetic anhydride.[17] The hydroperoxide (4·01 g.) contained in a dropping funnel fitted to the apparatus illustrated at the side-arm *D* was added to the acetate (2·26 g.) at *A*. The mixture was stirred at room temperature and 5·5 mm. for 8 hr.; acetic acid, probably mixed with the anhydride, collected in the cold trap. The excess of hydroperoxide was removed at 1 mm. and the residue sublimed in a high vacuum, then recrystallised from pentane, yielding *di-*(tert.-*butylperoxy*)*boron hydroxide,* m. p. 38—42° (Found: B, 5·2; peroxidic O, 30·9. $C_8H_{19}O_5B$ requires C, 5·25; peroxidic O, 31·1%).

Reaction of tert.-*Butyl Hydroperoxide with* o-*Nitrophenyl Dichloroboronite.*—*tert.*-Butyl hydroperoxide (3·336 g.) was added to the dichloroboronite [8] (4·078 g.) in methylene chloride at −40°. Volatile material was removed at 0·1 mm., yielding *di-*(tert.-*butylperoxy*)-o-*nitrophenoxyboron* as a red liquid (Found: C, 50·9; H, 6·65; peroxidic O, 18·3. $C_{14}H_{22}O_7NB$ requires C, 51·4; H, 6·78; peroxidic O, 19·3%).

Reaction of tert.-*Butyl Hydroperoxide with Di-*(o-*nitrophenyl*) *Chloroboronate.*—o-Nitrophenol (1·845 g.) in methylene chloride was added to the dichloroboronite (2·928 g.) in methylene chloride at −40°. After 1 hr. at room temperature, the hydroperoxide (1·195 g.) was added similarly, with cooling. Some *o*-nitrophenol was collected at 0·1 mm. on the cold-finger. The residue, a red liquid, m. p. *ca.* 15°, was tert.-*butylperoxydi-*(o-*nitrophenoxy*)*boron* (Found: C, 50·4; H, 4·5; peroxidic O, 8·35. $C_{16}H_{17}O_8N_2B$ requires C, 51·1; H, 4·5; peroxidic O, 8·5%).

[14] Davies, Foster, and White, *J.*, 1954, 2200.
[15] Parker, Ricciuti, Ogg, and Swern, *J. Amer. Chem. Soc.*, 1955, **77**, 4037.
[16] Abraham, Davies, Llewellyn, and Thain, *Analyt. Chim. Acta*, 1957, **17**, 499.
[17] Cook, Illet, Saunders, and Stacey, *J.*, 1950, 3125.

XUM

Reaction of Hydrogen Peroxide with Phenyl[^{18}O]*boronic Acid.*—A mixture of butyl phenylboronate [18] (20 g.; b. p. 136—138°/8—10 mm.) and [^{18}O]water (α 0·876) [19] was fractionally distilled; the water was recycled until all of the butanol had been collected (20 min.). The alcohol was isotopically normal. Cooling caused phenyl[^{18}O]boronic acid (9·8 g.) to separate.

This labelled boronic acid (1 g.) was stirred with 20 c.c. of a 6% solution of 100% hydrogen peroxide in [^{18}O]water. Heat was evolved as the solid dissolved in a few minutes. An ethereal extract yielded phenol which was isotopically normal.

Reaction of Hydroperoxides with Phenylboronic Acid.—(i) tert.-*Butyl hydroperoxide.* A solution of phenylboronic acid (1·35 g.) and *tert.*-butyl hydroperoxide (1 g.) in water (100 c.c.) was heated under reflux for 3 hr. An ethereal extract yielded phenol (tribromo-derivative, m. p. 93°).

(ii) 1 : 2 : 3 : 4-*Tetrahydro*-1-*naphthyl hydroperoxide.* A solution of the hydroperoxide (3·63 g.) and [^{18}O]boronic acid (2·7 g.) in [^{18}O]aqueous dioxan (4 : 1 by vol.) was kept at 25° for 72 hr. 1 : 2 : 3 : 4-Tetrahydro-1-naphthol (1·0 g.) of normal isotopic composition was isolated, having b. p. 255°, n_D^{25} 1·5625 (phenylurethane, m. p. and mixed m. p. 122°).

(iii) (−)-1-*Phenylethyl hydroperoxide.* The hydroperoxide [11] (1·195 g.), $\alpha_D^{16\cdot5}$ −1·94°, and phenylboronic acid (1·12 g.) were dissolved together in ether (20 c.c.). After 3 days the precipitated boric acid was removed by filtration; distillation yielded (−)-1-phenylethanol, b. p. 86°/15 mm., n_D^{25} 1·5279, α_D^{20} −0·66°.

Reaction between tert.-*Butyl Hydroperoxide and Hexylboron Difluoride.*—Hexylboron difluoride [20] (2·37 g.) was distilled in dry nitrogen into a mixture of *tert.*-butyl hydroperoxide (3·51 g.) and pentane (5 c.c.) at 0° in the apparatus illustrated. Reaction was vigorous and the mixture became coloured. After removal of the pentane at 30 mm. liquid was collected at 0·5 mm. in the cold-trap. Redistillation of the liquid gave di-(*tert.*-butyl) peroxide, b. p. 112°, which was identified by vapour-phase chromatography.[16] The residue in the still was hydrolysed and extracted with light petroleum. Treatment of the extract with α-naphthyl *iso*cyanate gave *n*-hexyl α-naphthylurethane, m. p. and mixed m. p. 59°.

We are indebted to Professors E. D. Hughes, F.R.S., and Sir Christopher Ingold, F.R.S., for their interest and encouragement, to Dr. G. A. Bunton and Professor D. R. Llewellyn for the isotopic measurements, and to Dr. J. Artozoul of the Institut Français du Pétrole for preparing the labelled phenylboronic acid. This work was carried out during the tenure of a D.S.I.R. Fellowship by R. B. M.

UNIVERSITY COLLEGE, GOWER ST., LONDON, W.C.1. [*Received, February 3rd,* 1958.]

[18] Bean and Johnson, *J. Amer. Chem. Soc.*, 1932, **54**, 4415; Brindley, Gerrard, and Lappert, *J.*, 1955, 2956.
[19] Bassey, Bunton, Davies, Lewis, and Llewellyn, *J.*, 1955, 2471.
[20] McCusker and Glunz, *J. Amer. Chem. Soc.*, 1955, **77**, 4253.

XUM

475. *Kinetics, Mechanism, and Chemistry of the Thermal Decomposition of Ammonium Dichromate.*

By JOHN SIMPSON, DUNCAN TAYLOR, and (in part) D. M. W. ANDERSON.

Kinetics of the decomposition *in vacuo* of well-formed single crystals of ammonium dichromate at 180—215° showed three consecutive processes: (1) an induction period corresponding to nucleation, (2) an autocatalysis consistent with a Prout–Tompkins chain mechanism, and (3) a constant-area interface process. In (2) the symmetry of the sigmoid pressure–time and weight decrease–time curves leads to a single value of the rate constant in the Prout–Tompkins equation in contrast to the two values required for other substances. During decomposition, the crystals became deep red, then gradually darkened owing to large numbers of submicroscopic nuclei to a highly cracked black solid amorphous to *X*-rays. In addition, a few black diamond-shaped nuclei developed on the crystal surfaces but only in the early stages, and were responsible for a very small fraction of the total decomposition. The induction period for crystals kept in a desiccator over phosphoric oxide decreased with increasing storage time, becoming zero after two years, and the acceleration stage of the autocatalysis then corresponded to spherical growth of a constant number of nuclei. These effects of ageing are compared with those in mercury fulminate. The equation for the reaction at 195·5° was determined; the composition of the black solid corresponded formally to $Cr_2O_3,0{\cdot}88H_2O,0{\cdot}047N_2O,0{\cdot}15O_2$. Nitrogen, nitrous oxide, and water were evolved throughout the reaction, but evolution of ammonia ceased after the autocatalytic stage. When prepared at 215°, the black solid contained no nitrous oxide but the same amount of extra oxygen, and its decomposition at 220—385° suggested that the extra oxygen was present as Cr_2O_5. Infrared spectra showed the formation of an intermediate which may contain nitrite and nitrate groups and reaches a maximum concentration at the end of the autocatalysis. Further evidence in support of an intermediate has been obtained from electrical-conductivity changes during decomposition of highly compressed pellets of the dichromate. A possible structure is suggested for it.

THERMAL decomposition at 195—218° of very small, rapidly grown crystals of ammonium dichromate occurs [1] in two main stages: (1) an autocatalytic stage best represented by the modified Prout–Tompkins equation [2] $\log_{10} p/(p_t - p) = k \log_{10} t + \text{const.}$, where p_t is the pressure, at the end of the stage, of gaseous products not absorbed by phosphoric oxide, followed by (2) a process of constant rate at an interface. We further investigated the decomposition in view of (*a*) the difference between these results and those of Fischbeck and Spingler [3] who reported a contracting-sphere mechanism [4] for most of the decomposition, (*b*) the failure to secure 100% decomposition according to their reaction scheme [5] $(NH_4)_2Cr_2O_7 \longrightarrow Cr_2O_3,H_2O + 3H_2O + N_2$, and (*c*) the conflicting reports [6] as to the nature of the gaseous and solid products. Kinetic measurements on well-formed single crystals were supplemented by microscopical observations, analysis of products, and measurements of electrical conductivity and infrared absorption.

EXPERIMENTAL AND RESULTS

Growth of Crystals.—Single crystals free from striae and growth steps were obtained as rhombs or hexagonal tablets of weight 5—20 mg. by slow evaporation in air at room temperature of solutions initially saturated with the " AnalaR " salt at 30°. The first crop, consisting

[1] Taylor, *J.*, 1955, 1033.
[2] Prout and Tompkins, *Trans. Faraday Soc.*, 1946, **42**, 468.
[3] Fischbeck and Spingler, *Z. anorg. Chem.*, 1939, **241**, 209.
[4] Garner, " Chemistry of the Solid State," Butterworths, London, 1955, p. 202.
[5] Fischbeck and Spingler, *Z. anorg. Chem.*, 1938, **235**, 183.
[6] (*a*) Moles and Gonzalez, *Anales Fis. Quim.*, 1923, **21**, 204; (*b*) Ball, *J.*, 1909, 87; (*c*) Ref. 5; (*d*) Harbard and King, *J.*, 1938, 955.

invariably of large, very imperfect crystals, was filtered off; the subsequent crop contained many small crystals from which suitable specimens were selected by hand with the aid of a lens. The crystals were dried by gentle pressure between filter papers, and either used immediately or stored in a desiccator over phosphoric oxide. Only very rarely were good crystals heavier than 20 mg. obtained. Fresh crystals, after being crushed and dried at 100°, lost 0·5% in weight. For comparative kinetic experiments, a few crystals, visibly very imperfect, of about 10 mg. were rapidly grown by the procedure in ref. 1.

Preparation of Pellets.—For electrical-conductivity measurements, and some thermal decompositions, ground recrystallised $(NH_4)_2Cr_2O_7$ was compressed at about 3 tons/sq. inch into strong hard cylindrical pellets, 6·52 mm. in diam. and 2—3 mm. in height, in which spurious electrical effects due to poor contacts between individual particles [7] were probably minimised.

Microscopical Observations.—Crystals, when heated from 170° to 230° on a hot-stage microscope either in air or in a small evacuated tube provided with a flat window, showed two phenomena: (1) surface growth of small black diamond-shaped nuclei whose long diagonals were always parallel to the *b* axis of the crystals; these diagonals were characterised by a pronounced crack with several others approximately at right-angles; (2) irreversible deep-red coloration throughout the crystal, followed by gradual darkening due to submicroscopic diffuse nuclei [8] to give finally a black lustrous solid of essentially the same shape as the original crystal; the final solid was riddled with cracks mostly aligned parallel to the original *b* axis. Occasionally, depending on the rate of heating and size of the crystals, the latter shattered into two or three pieces during decomposition. *X*-Ray measurements with single crystals showed that the colour change to deep red was not due to a polymorphic transformation. The diamond-shaped nuclei never developed to cover more than half of the surface before the darkening had rendered the crystal completely black and opaque. Experiments at 195·5° in the thermal decomposition apparatus showed that the opaque stage was reached at about 15% decomposition and, since the diamond-shaped nuclei appeared only on the surface, the main decomposition was apparently associated rather with the darkening process than with the discrete nuclei.

Nature of the Gaseous Products.—Sufficient ammonium dichromate was decomposed slowly at 196° in a small evacuated tube attached to a liquid-nitrogen trap to give a non-condensable gas of pressure 10 mm. Hg, the volume being 70 c.c. By gas chromatography on a silica gel column with nitrogen as the carrier gas and a thermal conductivity gauge as detector, the non-condensable gas was also found to be nitrogen. On flushing the condensate in the trap into the column, appreciable quantities of nitrous oxide were found; its identity was further confirmed by its infrared absorption. Water and ammonia were detected in the trap in a separate experiment by standard tests. No other gaseous product was found unless the dichromate was allowed to decompose explosively at higher temperatures, in which case with a charcoal column a little nitric oxide was detected also. Furthermore, in the liquid-nitrogen trap at the end of some of the weight-loss experiments with 100 mg. of dichromate, coupling tests [9] detected less than 5 μg. of nitrite and nitrate ions.

Procedure for Thermal Decomposition.—(1) The apparatus used to determine the kinetics of evolution of the gaseous products at 188—215° was similar to that described.[1] All samples, normally single crystals (5—20 mg.), were evacuated overnight at less than 10^{-6} mm. Hg before decomposition. At a given temperature, very similar pressure–time curves were obtained whether the platinum bucket containing the sample was loosely closed or left open. In experiments with a phosphoric oxide trap immediately following the reaction vessel to absorb water and ammonia, the combined pressure of nitrogen and nitrous oxide was measured (not nitrogen alone as previously believed [1]), while in others use of a liquid-nitrogen trap condensed all gases except nitrogen. The volume of the system could be varied between 600 and 6684 c.c. so that the final pressure was normally about 0·1 mm. Hg after 24 hr. Replacement of the McLeod by a Bourdon gauge and omission of cold and absorption traps allowed the pressure of the total gaseous products to be measured in a system of volume 600 c.c. which gave a final pressure of about 3 mm. Corrections to the measured pressures to allow for temperature differences in the system were calculated to be of similar size to the experimental errors, and were therefore omitted.

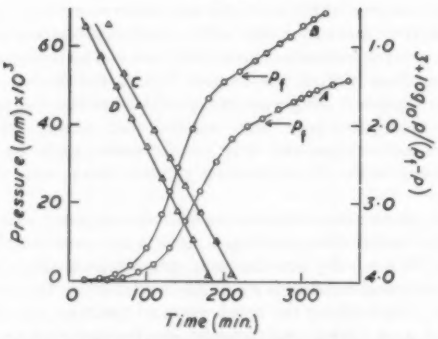
[7] Wagner and Hantlemann, *J. Chem. Phys.*, 1950, **18**, 72.
[8] Ref. 4, p. 187.
[9] Rider and Mellon, *Analyt. Chem.*, 1946, **18**, 96; Woodward, *Analyst*, 1953, **78**, 727.

XUM

The rate of evolution of ammonia at 195·5° was determined by decomposing about 0·5 g. of crystals in five successive stages with a liquid-nitrogen trap after the reaction vessel. The autocatalytic part of the decomposition was divided, by use of measurements of nitrogen pressure, into four roughly equal stages, while the fifth stage included the remainder of the decomposition up to a maximum time of 24 hr. After each stage the reaction was halted by raising the sample to the cold part of the reaction vessel, and the ammonia in the trap was then determined by addition, while the trap was still cold, of excess of hydrochloric acid and back-titration with sodium hydroxide solution.

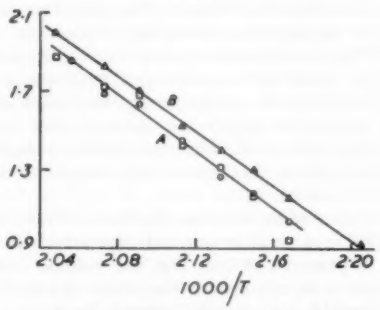
(2) To follow the loss in weight of the solid during decomposition, a McBain–Bakr balance was used, the spring being of 0·25 mm. diam. beryllium–copper wire. The sample, in a platinum-foil bucket, was suspended in the hot zone of the reaction vessel near a thermocouple by means of a 30 cm. fine glass rod attached to the spring, whose extension was observed with a microscope provided with an eyepiece scale. The sensitivity of the balance required a sample weight of about 100 mg. (several crystals or a small pellet) and the useful temperature range was 188—200°. Above 200° the rapid rate and occasional splitting of the crystals caused violent oscillation of the spring so that rate measurements were impossible. After raising the electric furnace round the reaction vessel the heating period was not less than 30 min., but

FIG. 1.



Curves *A* and *B*: Pressure–time curves for evolution of N_2 and $N_2 + N_2O$ respectively at 195·5°. Lines *C* and *D*: Prout–Tompkins equation plots for curves *A* and *B* respectively.

FIG. 2.



Line *A*: Activation-energy plot for autocatalytic stage: ○ N_2 runs, □ $N_2 + N_2O$ runs. Vertical axis $3 + \log_{10} k$. Line *B*: Activation-energy plot for nucleation stage. Vertical axis $3 + \log_{10} 1/\tau$.

fortunately only a small fraction of the total (*ca.* 32%) decrease in weight occurred during this time. Experiments were conducted: (*a*) with continuous evacuation and a liquid-nitrogen trap between balance and pump, or (*b*) with the pressure of one or more of the gaseous products building up in the balance after preliminary evacuation to 10^{-3} mm. Hg. In (*b*), a liquid-nitrogen trap allowed only nitrogen to accumulate, while phosphoric oxide or barium oxide in a small dish placed just above the spring allowed nitrogen and nitrous oxide, or these and ammonia, respectively, to accumulate. Tests showed that barium oxide under the experimental conditions absorbed only minute traces of ammonia. The volume of the balance and trap being about 650 c.c., the final pressures reached in (*b*) were 10—20 mm. Hg.

Kinetics of Evolution of Nitrogen and of Nitrogen plus Nitrous Oxide.—Pressure–time curves for individual freshly prepared crystals were determined at seven temperatures between 188° and 215°. Despite great care in the selection of crystals, rates were reproducible generally only to within about 20%, so several runs were carried out at each temperature and the results averaged to determine activation energies. All pressures were corrected to a standard initial sample weight of 10 mg. and a reaction volume of 6684 c.c. by assuming direct proportionality between pressure and initial weight. This was justified by the observation at 195·5° that both the maximum rate in the autocatalytic stage and the later constant rate were directly proportional to the initial crystal weight over the range 2—20 mg. At a given temperature, the corrected pressures at any given stage in the decomposition were reproducible to better than 5%. For all experiments the pressure–time curves were very similar to those already

published [1] except that induction periods were much longer (10—70 min., decreasing with rise in temperature) and the sigmoid part of the curves could best be represented by the original Prout–Tompkins equation [10] $\log_{10} p/(p_f - p) = kt +$ const. where p_f is the pressure at the end of the sigmoid. Fig. 1 is typical for these experiments and shows that a single value of k is required for the whole of the sigmoid in both the N_2 and $N_2 + N_2O$ runs, in contrast to the two values found in other decompositions.[11] A single value for k requires the sigmoid curve to be symmetrical with the maximum rate at the mid-point; experimentally, these conditions were closely fulfilled. Mean values of $\log_{10} k$ are plotted in Fig. 2, line *A*, which leads to an activation energy for both the N_2 and $N_2 + N_2O$ experiments of 33 ± 1·5 kcal./mole. Similar plots of the constant rates gave an activation energy of 41 ± 2 kcal./mole both for evolution of N_2 and for that of $N_2 + N_2O$. In the nitrogen runs, irrespective of temperature, the final pressure after 24 hr. corresponded to 54 ± 2% of the theoretical nitrogen in the dichromate and p_f to 38 ± 2%. For $N_2 + N_2O$, the final pressure at 188° was equivalent to 73 ± 2% of the theoretical nitrogen content, and rose to 83 ± 2% at 205°, remaining constant thereafter up to 215°. Thus 19—29% ±4% of the nitrogen in the dichromate was evolved as nitrous oxide, and the increase with rising temperature was due mainly to extra gas evolved during the indeterminate decay stage which followed the constant-rate process. The average of several

FIG. 3. *Evolution of nitrogen and ammonia at 195·5°.*

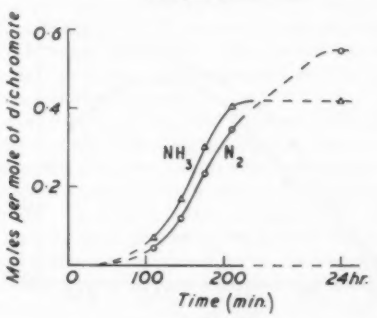
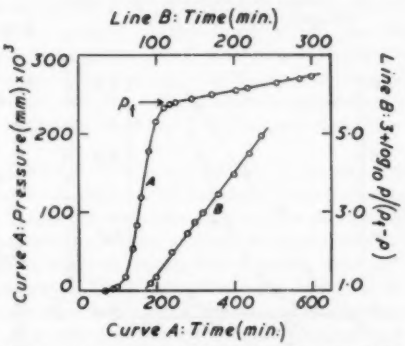


FIG. 4.



Curve *A*: Pressure–time curve for evolution of total gases at 195·5°. Line *B*: Prout–Tompkins equation plot for curve *A*.

experiments at 195·5° showed that 0·54 mole of nitrogen and 0·24 mole of nitrous oxide were obtained from each mole of dichromate. Attempts to construct reliable nitrous oxide pressure–time curves by taking the difference between the pressures of corresponding $N_2 + N_2O$ and N_2 curves failed: it was impossible to relate accurately the time scales of separate experiments owing to the difficulty of determining induction periods to better than ±5 min. Interruption of the decomposition (cf. ammonia determinations) during either the autocatalytic or constant-rate stages did not influence the shape of the nitrogen pressure–time curve provided allowance was made for the short heating periods, thus showing that energy chains were absent.[12]

Rapidly grown crystals gave much faster and less reproducible rates and, as earlier found,[1] the modified Prout–Tompkins equation [3] (*i.e.*, with $\log_{10} t$ in place of t) gave the best fit for the autocatalytic stage.

Evolution of Ammonia and Water.—Typical results for a stepwise decomposition at 195·5° (Fig. 3) show that virtually all the ammonia is evolved during the autocatalysis. The average of four experiments gave the total ammonia as 0·41 mole per mole of dichromate. The total loss in weight of the dichromate, less the weight of ammonia and of nitrogen and nitrous oxide determined above, corresponded to 2·6 moles of water per mole of dichromate. Attempts to determine the water by weighing the contents of the trap and allowing for the condensed

[10] Prout and Tompkins, *Trans. Faraday Soc.*, 1944, **40**, 488.
[11] Tompkins and Young, *Ann. Reports*, 1953, **50**, 73, 77, 79.
[12] Ref. 4, p. 195; Tompkins and Young, *Trans. Faraday Soc.*, 1956, **52**, 1245.

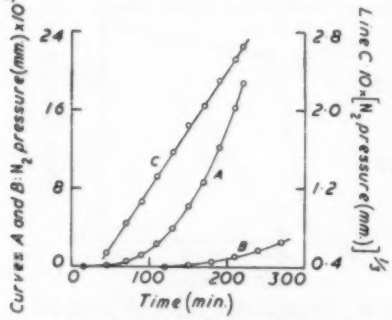
XUM

ammonia and nitrous oxide gave undoubtedly high results, owing probably to distillation into the trap of small unknown weights of mercury from the McLeod gauge.

Kinetics of Evolution of Total Gaseous Products.—Typical results at 195·5° are given in Fig. 4, in which pressures have been corrected as in the nitrogen-evolution runs. Notable features are the very good fit of the Prout–Tompkins equation for the autocatalytic stage, and the extension of the constant-rate stage to about 6 hr. compared with about 2 hr. for N_2 and $N_2 + N_2O$ experiments. Comparison with curves for the other gases showed that water, in contrast to ammonia, was evolved throughout the decomposition, but totalled only 2·0 moles per mole of dichromate instead of 2·6 moles as calculated above. In view of the low partial pressures involved, the loss is believed to be due to adsorption on the glass surfaces, and the value 2·6 is preferred.

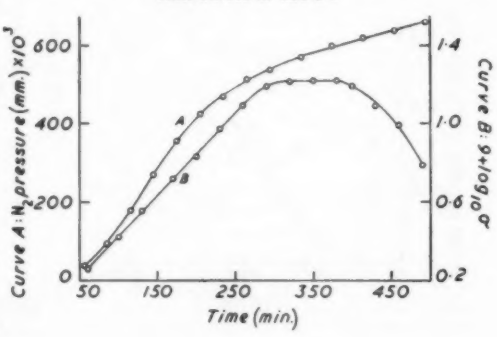
The Induction Period.—Induction periods were arbitrarily defined as the time τ (min.) required for the nitrogen pressure to reach 10^{-4} mm. Hg, the rate during the period being taken as $1/\tau$. For well-formed freshly grown crystals, values of τ showed considerable scatter, but mean values at a given temperature did not appear to be influenced significantly by crystal habit or weight, and the temperature coefficient of $1/\tau$ gave an activation energy of 32 $\pm$ 1 kcal./mole (Fig. 2, line *B*). At the end of the induction period, crystals were very deep red, and after 1% decomposition had perceptibly darkened but no diamond-shaped nuclei had appeared. *X*-Ray

FIG. 5. *Change in kinetics at* 180·5° *after storage over phosphoric oxide.*



Curves *A* and *C*: Crystal stored for 2 years.
Curve *B*: Freshly prepared crystal.

FIG. 6. *Nitrogen pressure–time and specific conductivity–time curves at* 186·3°.



rotation photographs of a crystal before and after 1% decomposition were identical. Rapidly grown crystals gave much shorter, and sometimes zero, values of τ. Saturated ammonium dichromate solutions, after exposure to daylight for several weeks at room temperature, were noticeably darker in colour and yielded by slow growth dark red crystals which decomposed without an induction period. The fact that occasionally τ was zero showed that induction periods were not significantly affected by delays in the diffusion of gaseous products from the reaction vessel to the rest of the system. Qualitative measurements of the visible absorption spectrum of crystals with a Unicam S.P. 600 spectrophotometer showed that no new absorption bands in the range 5500—10,000 Å appeared either during the induction period or after short decomposition at 195·5°. Well-formed, sufficiently thin crystals could not be obtained to permit measurements below 5500 Å where the absorption is very strong.[13]

Effect of Ageing over Phosphoric Oxide.—Well-formed crystals, when stored over phosphoric oxide, progressively lost their original brilliance, edges and corners became slightly rounded, and the induction period at 180·5° decreased from 120 min. to zero after 2 years' storage. At 180·5° the acceleration part of the autocatalysis for a 2 years-old crystal was faster than that for a new one (see Fig. 5, where pressures have been corrected as in the nitrogen-evolution runs), and best fitted the relation $p(N_2) \propto t^3$ as far as the maximum-rate stage (35% decomposition). Crystals up to 1 year old yielded the relation $p(N_2) \propto t^n$ up to 20—25% decomposition over a range of temperatures, n varying between 2·5 and 5·5. The decay part of the sigmoid curve

[13] Englis and Wollerman, *Analyt. Chem.*, 1952, **24**, 1983.

always fitted the Prout–Tompkins equation with the same value of k as for un-aged crystals at the same temperature. The constant rates for aged crystals were less reproducible than for new crystals, but age had no significant effect on the percentage decomposition at the end of either the sigmoid or the constant-rate stages.

Effect of Ultraviolet and γ-Irradiation.—Exposure of crystals in air to ultraviolet light for several hours had no detectable effect. Crystals after exposure *in vacuo* for 4 months to ^{60}Co γ-rays of low intensity had become very dark red, and gases were evolved up to a point corresponding to not more than the end of an induction period. However, on subsequent thermal decomposition at 195·5°, an induction period only slightly less than normal occurred and, while the autocatalytic stage fitted the Prout–Tompkins equation, two values of k were required: 0·023 up to the maximum-rate stage and 0·015 thereafter, compared with 0·0175 for the single k of un-irradiated crystals at the same temperature.

Loss-in-weight Studies.—Experiments at four temperatures between 188° and 200° with continuous evacuation gave weight decrease–time curves having the same features as the pressure–time curves in Fig. 1, but rates were generally less reproducible. The autocatalysis could again best be represented by the Prout–Tompkins equation with a single value of k and had an activation energy of 35 ± 3 kcal./mole. For the constant-rate stage the activation energy was 41 ± 3 kcal./mole. Decomposition of pellets gave similar curves and no evidence for a contracting-cylinder type of process.[14] Slight but distinct catalysis of the decomposition in the early stages by the black solid product was observed with a pellet prepared from an intimate mixture of the dichromate with 10% by weight of the black solid. At 192°, decompositions where one or more of the gaseous products accumulated showed that the reaction was not inhibited by nitrogen or nitrous oxide, but was inhibited appreciably by ammonia and very strongly by water. Since inhibition was absent from the total-pressure experiments and the final pressures were about 3 mm. Hg, pressures greater than the latter appear necessary to give a significant effect.

Composition of the Solid Products.—The final black solid obtained at 195·5°, although pseudomorphous with the original crystals, was amorphous to X-rays. The chromium was determined volumetrically after fusion with sodium peroxide,[15] and the water by roasting the solid at 800° *in vacuo* in a silica tube attached to a phosphoric oxide tube, whose increase in weight was noted (Found: Cr, 60·1%; H_2O, 8·1%). Two other gases evolved during the roasting were shown by gas chromatography to be nitrous oxide and oxygen. Their quantities were determined by heating the solid in the thermal decomposition apparatus and noting the pressures developed; a phosphoric oxide trap was used to absorb water and where necessary a liquid-oxygen trap to condense nitrous oxide. All the latter was evolved by 230°, but no oxygen until 385°, at which it was evolved explosively and then partially adsorbed on the solid (Found: N_2O, 1·2%; O_2, 2·8%). The black solid obtained at 215° was found on similar treatment to evolve no nitrous oxide but the same amount of oxygen. After treatment at 385° the solid contained 67·4% of chromium (Calc. for Cr_2O_3: 68·4%) and, as shown by X-ray powder photographs, had partially crystallised as Cr_2O_3.

After 20—30% decomposition at 195·5°, the dichromate was black to the eye but still partially soluble in water to give a greenish-yellow solution. Spectrophotometry [13] showed the solution to contain 1·5% of the total chromium as chromic ions. At the end of the autocatalytic stage (70% decomposition) the solid was completely insoluble in water. At no stage in the decomposition could any nitrite or nitrate ions be extracted from the solid with water, hydrochloric acid, or sodium hydroxide solution.

Electrical-conductivity Measurements.—The electrical equipment and conductivity cell were similar to those of Jacobs,[16] except that the direction of the applied potential (1—120 v D.C.) was reversed manually. Full details of the electrical circuit were given by Simpson.[17] The empty evacuated cell at 200° had a resistance greater than 10^{16} ohms, while the range of resistances measured for dichromate pellets was 10^7—10^{13} ohms. From 37° to 162° the specific conductivity of pellets *in vacuo*, after 24 hours' preliminary evacuation at room temperature, was given by $\sigma = 9{\cdot}4 \exp(-20{,}400/RT)$ ohm^{-1} cm.$^{-1}$ irrespective of the direction of the applied

[14] Cf. ref. 4, p. 200.
[13] Cumming and Kay, "Quantitative Chemical Analysis," Oliver and Boyd, Edinburgh, 10th edn., p. 140.
[16] Jacobs, *J. Sci. Instr.*, 1953, **30**, 204.
[17] Simpson, Ph.D. Thesis, University of Edinburgh, 1957.

XUM

voltage, results being reproducible within ±2%. Both the activation energy and the pre-exponential factor are reasonably characteristic of structure-sensitive conduction.[18] The fact that the same resistance values were obtained at corresponding temperatures on heating and cooling showed that the pellet had not significantly decomposed. Over the same range of temperature the activation energy for conduction was 12·4 ± 1 kcal./mole after the pellet had been allowed to decompose for 24 hr. at 180°.

By connecting the vessel containing the conductivity cell to the thermal-decomposition apparatus, conductivity–time and nitrogen pressure–time curves for dichromate pellets were determined simultaneously. The apparatus was evacuated for 24 hr. at room temperature before the furnace was raised round the reaction vessel, and since the cell was freely suspended in the vessel by a thin wire the heating period was about 40 min., compared with the total decomposition time of 12 hr. at 186·3°. At higher temperatures appreciable decomposition occurred during the heating, while below 180° the reaction was prohibitively slow. Results at 186·3° are shown in Fig. 6, the exponential rise in σ with time being typical for the ten pellets examined. At the same temperature, experiment with a thermocouple (48 gauge wire) embedded in a pellet showed that no self-heating occurred during decomposition.

Infrared-absorption Measurements.—A Hilger H 800 spectrophotometer with a rock-salt prism was used, calibration for frequency being carried out daily with polystyrene. An accuracy of ±2 cm.$^{-1}$ is claimed. Spectra were determined for ammonium dichromate before and after its complete decomposition (24 hr.) at 195·5°, and also at the end of each of seven roughly equally spaced stages in the reaction. New absorption peaks at 1270 and 825 cm.$^{-1}$ gradually developed, reached maximum intensity at the end of the autocatalytic stage, and then decayed to zero by the end of the decomposition. By the end of the autocatalytic stage the known strong peak of ammonium ions [19] at 3170 cm.$^{-1}$ had virtually disappeared, but a peak at 1385—1400 cm.$^{-1}$, initially strong and which is common to the ions NH_4^+, NO_3^-, and NO_2^-, retained a medium intensity. The latter peak was still evident, though very weak, even at the end of the decomposition. Spectra obtained from potassium bromide discs and Nujol mulls gave the same results. No evidence was obtained to suggest that any of the above peaks were due to adsorbed ammonia or nitrous oxide. For comparison, spectra of sodium nitrite and nitrate and ammonium nitrate were determined in potassium bromide discs and showed the following absorptions (cm.$^{-1}$, for s, m, w, see Table): NO_2^-: 2550 w, 1380 m, 1270 s; NO_3^-: 1385 s, 825 m; NH_4^+: 3170 s, 1400 s (cf. refs. 19, 20). Thus in the dichromate spectra the 1270 cm.$^{-1}$ peak suggests the formation of nitrite ion as one of the species in an intermediate product, while the 825 cm.$^{-1}$ peak (together with the persistence of the peak at 1385—1400 cm.$^{-1}$ after the disappearance of the peak at 3170 cm.$^{-1}$) suggests nitrate. It also seems likely that most of the ammonium ions have decomposed by the end of the autocatalysis. However, the failure to extract nitrite or nitrate ions from the solid products of decomposition shows that, if these ions are present, they do not occur in a soluble form and may therefore be strongly co-ordinated in the intermediate. Co-ordination should alter the absorption frequencies compared with those of the free ions,[21a] and in an attempt to elucidate the nature of the co-ordination, spectra of $[Cr(NH_3)_5H_2O](NO_3)_3,NH_4NO_3$ (*A*), $[Cr(NH_3)_5NO_2](NO_3)_2$ (*B*), $[Cr(NH_3)_5NO_2](NO_3)_2$ (*C*), and $[Cr(NH_3)_6](NO_3)_3$ (*D*) were determined in Nujol mulls. Peaks within the range obscured by Nujol absorptions were determined with potassium bromide discs and are marked with an asterisk. When the rock-salt plates were protected from the mulls with polystyrene films [21b] the spectra were unchanged. Results are given in the Table.

Frequency (cm.$^{-1}$, s = strong, m = medium, w = weak, v = very).

A	*B*	*C*	*D*	*A*	*B*	*C*	*D*
1763 w	1766 w	1765 w	1762 w	—	1228 s	—	—
1630 m	1628 m	1627 m	1633 m	1049 w	—	1054 vw	1038 m
—	1487* s	1501 s	—	—	1017 s	1022 s	—
1395* vs	1390* vs	1379* vs	1386* s	—	—	—	954 m
1312* s	1302* s	1309* s	1304* s	824 m	833 s	836 m	831 m
—	—	1277 s	—	753 s	772 s	781 s	779 s

[18] Jacobs and Tompkins, *Quart. Reviews*, 1952, **6**, 238.
[19] Miller and Wilkins, *Analyt. Chem.*, 1952, **24**, 1253.
[20] Weston and Brodasky, *J. Chem. Phys.*, 1957, **27**, 683.
[21] (*a*) Gatehouse, Livingstone, and Nyholm, *J.*, 1957, 4222; (*b*) Gatehouse, *Chem. and Ind.*, 1957, 1351.

Frequencies near 1620, 1310, and 770 cm.$^{-1}$ have been reported [22] for ammonia co-ordinated to Cr^{3+} ions, and those at 1530—1480, 1290—1250, and 1034—970 cm.$^{-1}$ are characteristic of nitrato-complexes.[21] If any nitrite or nitrate groups are present in the intermediate product, they appear not to be co-ordinated to Cr^{3+} normally. For *A*, *B*, *C*, and *D* several of the peaks in Nujol mull spectra were displaced by up to 18 cm.$^{-1}$ in spectra from potassium bromide discs.

Discussion

Reaction Kinetics.—The results for un-aged crystals in both the pressure–time and weight decrease–time experiments, together with the appearance of many cracks in the crystals during decomposition, confirmed the earlier view [1] that the autocatalytic stage is consistent with a branching and interfering chain mechanism of the Prout–Tompkins type with an activation energy of $33 \pm 1{\cdot}5$ kcal./mole. The chain process is followed by a reaction at an interface of constant area of significantly higher activation energy (41 ± 2 kcal./mole for single well-formed crystals and 38 ± 2 kcal./mole for small imperfect crystals [1]). In the autocatalysis the results fit the original Prout–Tompkins equation [10] better than the modified equation [2] required in the earlier work. (In the former equation, the chain-branching coefficient is assumed to be independent of time, and in the latter inversely proportional to it.) This feature may well be due to the use here of well-formed crystals where the slower rates and longer induction periods indicate fewer reaction chains, and where a more nearly constant branching coefficient would thus be expected. The pronounced extension of the constant-rate stage in the total-pressure experiments suggests that at low pressures water and ammonia act to preserve the reaction interface of constant area, although the weight-decrease experiments clearly showed that at higher pressures water, and to a smaller extent ammonia, inhibit the decomposition. Since, except for the ammonia determinations, the different types of kinetic experiment gave very similar results, it appears that nitrogen, nitrous oxide, and water are all formed in one set of chemical processes during the autocatalysis and in a different set during the constant-rate stage. The reactions giving free ammonia are probably quite different although the corresponding activation energy is unknown.

The two main stages of the reaction discussed above are preceded by a nucleation stage, and in spite of the considerable scatter in induction periods, the activation energy of the stage is believed to be 32 ± 1 kcal./mole. The latter, being not greater than the values for the other two stages (the pre-exponential factors are unknown), is consistent with the observation that by far the greater part of the decomposition is associated with a general darkening of the solid by large numbers of diffuse nuclei rather than with the growth of relatively few discrete nuclei.[8] The amount of decomposition caused by γ-irradiation of crystals was very small owing partly to the relatively low dose rate, and although the induction period in the subsequent thermal decomposition was only slightly reduced compared with that in un-irradiated crystals, the probability of chain branching in the acceleration stage (given by k in the Prout–Tompkins equation) had increased significantly.

The kinetics found for fully aged single crystals up to the maximum-rate stage suggest spherical growth of a constant number of nuclei. This change in kinetics compared with those for fresh crystals is parallel to that found when mercury fulminate is aged [23] and may have a similar explanation: ageing is considered to change the grain structure of the crystals as a result of slight decomposition such that a large number of non-contiguous blocks are formed, thus preventing the propagation from block to block of the reaction chains which give rise to Prout–Tompkins kinetics. The cubic relation then describes the kinetics of the reaction occurring in the individual blocks. However, with ammonium dichromate, in contrast to the fulminate, no decomposition could be detected during

[22] Kobayashi and Fujita, *J. Chem. Phys.*, 1955, **23**, 1354; Svatos, Sweeny, Mitzushima, Curran, and Quagliano, *J. Amer. Chem. Soc.*, 1957, **79**, 3313.
[23] Bartlett, Tompkins, and Young, *J.*, 1956, 3323; Tompkins and Young, *Discuss. Faraday Soc.*, 1957, **23**, 202.

XUM

ageing, but only a change in the physical appearance of the crystals. We suggest therefore that the structural change may have been due to the loss of traces of water (and maybe of ammonia) during storage over phosphoric oxide. This would imply either that chain branching across blocks in un-aged crystals occurs *via* water and/or ammonia molecules, or that loss of traces of these molecules from grain boundaries results in the collapse of bridges composed essentially of dichromate molecules. Since, after the maximum rate stage, the decay part of a normal Prout–Tompkins chain process occurred, it may be either that ageing did not affect the whole crystal, or that, on heating, a type of annealing process involving the reaction products water and ammonia took place, so that continuity between the blocks was restored.

Chemistry of the Decomposition.—The equation for the decomposition at 195·5° can be written as

$$(NH_4)_2Cr_2O_7 \longrightarrow \text{Black solid} + 0{\cdot}54N_2 + 0{\cdot}24N_2O + 0{\cdot}41NH_3 + 2{\cdot}6H_2O,$$

the loss in weight of the dichromate being close to 32%. The black solid formed at the same temperature can be shown to correspond formally to $[Cr_2O_3,0{\cdot}88H_2O,0{\cdot}047N_2O,0{\cdot}15O_2]$; it loses 12% in weight when roasted to give essentially chromic oxide. Calculation showed that the nitrogen balance for the reaction is correct to within 3%; in view of the experimental errors this is satisfactory and shows that no significant nitrogen-containing product has been missed.

The above equation shows that approximately one in every five ammonium ions decomposes to give free ammonia, probably by the reactions (cf. ammonium perchlorate [24]):

$$NH_4^+ + Cr_2O_7^{2-} \longrightarrow NH_4 + Cr_2O_7^- \longrightarrow NH_3 + HCr_2O_7^-$$

Since virtually all of the ammonia is evolved during the autocatalytic stage, and in view of the infrared absorption data, the other 80% of the ammonium ions have probably been oxidised in other ways before the end of the stage, though the solid must still possess a source of hydrogen (perhaps as NH_2 groups) because water continued to be evolved up to the end of the decomposition.

Infrared absorptions indicate the formation of an intermediate which may contain nitrite and nitrate groups and whose concentration reaches a maximum by the end of the autocatalysis, the solid then being completely insoluble. Since it seems most unlikely that ammonium nitrite or nitrate could be present in the decomposing solid, it is suggested that the intermediate consists of chains of alternating chromium and oxygen atoms to which nitrite and nitrate (and maybe NH_2) groups are linked (cf. ref. 25). The formation of such a chain structure seems reasonable in view of the occurrence in the original salt of chains of dichromate ions with ammonium ions conveniently placed near the ends of the former ions.[26] Although nitrogen, nitrous oxide, and water are evolved at all stages of the decomposition, the formation of the intermediate evidently predominates during the autocatalytic stage, and its decomposition during the subsequent stages. The evidence for the slight occurrence of $Cr_2O_7^{2-} \longrightarrow Cr^{3+}$ in the early stages of the decomposition suggests that Cr^{3+}, which can be extracted with water, may also be a transient intermediate, but one whose concentration is always low. On the other hand, the Cr^{3+} may have arisen indirectly *via* the soluble Cr_3O_8 [27] produced by decomposition of the acid which is formed when ammonia is evolved. The infrared spectrum of the final black solid obtained at 195·5° indicates the presence of a small concentration of nitrate groups but the absence of nitrite; and since the solid when further heated yields a little nitrous oxide, the latter may arise preferentially from reactions of the nitrate groups and nitrogen from the

[25] Bircumshaw and Newman, *Proc. Roy. Soc.*, 1955, *A*, **227**, 228.
[26] Schmitz-Du Mont, *Z. Elektrochem.*, 1956, **60**, 866; Bailar, "Chemistry of the Coordination Compounds," Reinhold, New York, 1956, p. 448.
[27] Byström and Wilhelmi, *Acta Chem. Scand.*, 1951, **5**, 1003.
[27] Schwartz, Fankuchen, and Ward, *J. Amer. Chem. Soc.*, 1952, **74**, 1676.

nitrite (and/or NH_2) groups. The electrical conductivity of pellets during decomposition suggests the exponential production with time of current carriers which are later destroyed, and may therefore be related to the intermediates discussed above.

The explosive evolution of oxygen at about 385° from the black end-product is characteristic of the decomposition of the oxide Cr_2O_5,[6d,28] which may thus be one of the decomposition products of the intermediates or of the acid formed when ammonia is evolved. The quantity of oxygen evolved shows that the black solid may contain about 16% by weight of Cr_2O_5. After roasting of the black solid, the green product, in view of its high oxygen content compared with Cr_2O_3, may contain about 10% by weight of CrO_2, because the limits of deficiency or excess of oxygen in Cr_2O_3 are very narrow.[29]

Acknowledgments are given to Dr. T. Moeller for preparative details of the complex chromium compounds, to Drs. C. A. Beevers and H. Ehrlich for assistance with the *X*-ray measurements, to Dr. J. Falconer for guidance on gas chromatography and to this University for a Research Studentship (to J. S.).

CHEMISTRY DEPARTMENT,
UNIVERSITY OF EDINBURGH. [*Received, February 3rd,* 1958.]

[28] Glemser, Hauschild, and Trupel, *Z. Anorg. Chem.*, 1954, **277**, 113.
[29] Bevan, Shelton, and Anderson, *J.*, 1948, 1729.

---

476. *The Mechanism of* N-*Acylation of* 2-*Mercaptoglyoxalines.*

By J. A. BAKER.

Reaction of 2-ethylthio-1-methylglyoxaline (II; R = Et) with ethyl iodide gives a quaternary salt, which yields 1-ethyl-2 : 3-dihydro-3-methyl-2-thioglyoxaline (III; R = Et) when heated. Evidence is given that *N*-ethoxycarbonylation of 2-mercapto-1-methylglyoxaline (I) in basic media follows a similar route, but the intermediate salt is less stable. Thermal decarboxylation of 1-ethoxycarbonyl-2 : 3-dihydro-3-methyl-2-thioglyoxaline gives both 2-ethylthio-1-methylglyoxaline and 1-ethyl-2 : 3-dihydro-3-methyl-2-thioglyoxaline. 2-Ethoxycarbonylthio-1-methylglyoxaline hydrochloride yields only 2-ethylthio-1-methylglyoxaline.

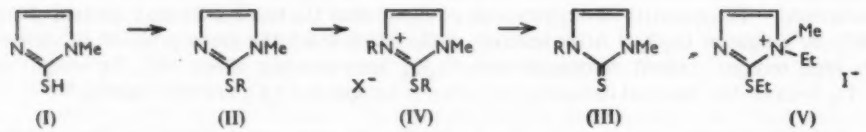
EARLIER confusion concerning the structures of the compounds obtained by the acylation of 2-mercaptoglyoxalines was resolved by Lawson and Morley [1] who showed that acylation in non-basic media gives *S*-acyl and in basic media gives *N*-acyl products. They concluded from spectroscopic evidence that 2-mercaptoglyoxalines exist mainly in the thione form in neutral solution, the thiol–thione equilibrium being altered in favour of the thiol in alkaline solution. In order to explain the anomalous formation of *N*-acylated compounds in aqueous sodium hydroxide, that is, under conditions which would seem to favour *S*-acylation, migration of the acyl group of the first-formed *S*-acyl compound from sulphur to nitrogen was postulated.

2-Mercapto-1-methylglyoxaline (I) with ethyl chloroformate in acetone gives the hydrochloride of 2-ethoxycarbonylthio-1-methylglyoxaline (II; R = CO_2Et). Reaction in pyridine or aqueous sodium hydroxide gives 1-ethoxycarbonyl-2 : 3-dihydro-3-methyl-2-thioglyoxaline (III; R = CO_2Et). The latter compound is also formed rapidly when the hydrochloride of the *S*-ethoxycarbonyl compound (II; R = CO_2Et) is treated with pyridine, but when aqueous sodium hydroxide is used the liberated base shows little tendency to rearrange spontaneously. Therefore, spontaneous migration of the ethoxycarbonyl group cannot be part of the reaction mechanism when the acylation is carried out in aqueous sodium hydroxide.

[1] Lawson and Morley, *J.*, 1956, 1103.

XUM

2-Mercapto-1-methylglyoxaline (I) with ethyl iodide in non-basic media yields 2-ethylthio-1-methylglyoxaline (II; R = Et) as its hydriodide.[2] If the base is now liberated from its salt, it will react with a second molecule of ethyl iodide to form 1-ethyl-2-ethylthio-3-methylglyoxalinium iodide (IV; R = Et, X = I) [a lower-melting compound is also formed, possibly the unsymmetrical isomer (V)]. This compound loses ethyl iodide



(I) (II) (IV) (III) (V)

at its melting point, but the ethyl group evolved is the one which was attached to sulphur, the product being 1-ethyl-2 : 3-dihydro-3-methyl-2-thioglyoxaline (III; R = Et). This is a neutral compound which forms no picrate. It has strong absorption at 2600 Å, characteristic of the thione group in this environment.[1] With ethyl iodide, the ethiodide (IV; R = Et, X = I) is re-formed.

By analogy, it seemed possible that the formation of a corresponding, but less stable, quaternary compound was an intermediate stage in the rearrangement of the 2-acylthioglyoxalines. In support of this hypothesis it was found that addition of a trace of ethyl chloroformate to an ethereal solution of 2-ethoxycarbonylthio-1-methylglyoxaline (II; R = CO_2Et) caused the rapid formation of the *N*-ethoxycarbonyl compound (III; R = CO_2Et), whereas three weeks were required before an untreated solution showed signs of rearrangement. Rearrangement of the *S*-ethoxycarbonyl compound was also catalysed, but less effectively, by the hydrochlorides of organic bases; pyridine hydrochloride was the most effective of those tried and 2-ethoxycarbonylthio-1-methylglyoxaline hydrochloride the least effective. Free pyridine slightly accelerated the rearrangement. Ammonium chloride was ineffective. The mechanism of this catalysis is not apparent.

The quaternary compound (IV; R = CO_2Et, X = Cl) is apparently re-formed in the presence of excess of ethyl chloroformate. When the resulting solution is warmed, decarboxylation takes place until all the ethyl chloroformate has decomposed, the 1-ethoxycarbonyl-2 : 3-dihydro-3-methyl-2-thioglyoxaline (III; R = CO_2Et) being recovered.

It is concluded that the first product of the reaction of 2-mercaptoglyoxalines with ethyl chloroformate is an *S*-ethoxycarbonyl compound in basic and non-basic media. In non-basic media, this exists as a hydrochloride which resists further attack by the reagent. In basic media, the free base is formed, which reacts with more ethyl chloroformate to form a quaternary compound. This is unstable and splits off the ethoxycarbonyl group from the sulphur atom as ethyl chloroformate, giving an *N*-ethoxycarbonyl compound as the final product.

Rearrangement of an ethoxycarbonyl group from sulphur to nitrogen is also known for thioureas. Dixon and his co-workers[3] isolated an unstable bicarbonate as an intermediate product in this rearrangement when sodium hydrogen carbonate was used to liberate the free base.

It has been reported that 1-ethoxycarbonyl-[1] and 4-ethoxycarbonyl-2-mercaptoglyoxalines[4] give 2-ethylthioglyoxalines when heated. When 1-ethoxycarbonyl-2 : 3-dihydro-3-methyl-2-thioglyoxaline (III; R = CO_2Et) was heated above its melting point the major product was 2-ethylthio-1-methylglyoxaline (II; R = Et), but some 1-ethyl-2 : 3-dihydro-3-methyl-2-thioglyoxaline (III; R = Et) was also formed. The hydrochloride of 2-ethoxycarbonylthio-1-methylglyoxaline (II; R = CO_2Et) also gave 2-ethylthio-1-methylglyoxaline when heated but no *N*-ethyl derivative was obtained.

[2] Marckwald, *Ber.*, 1892, **25**, 2354.
[3] Dixon *et al.*, *J.*, 1920, **117**, 80, 720.
[4] Jones, *J. Amer. Chem. Soc.*, 1952, **74**, 1084.

Experimental

2-Ethoxycarbonylthio-1-methylglyoxaline Hydrochloride.—Ethyl chloroformate (12 g., 0·11 mol.) was added dropwise with stirring to 2-mercapto-1-methylglyoxaline (11·4 g., 0·1 mol.) in acetone (50 ml.) under reflux during 10 min. and heating continued for a further 10 min. Cooling and seeding afforded *2-ethoxycarbonylthio-1-methylglyoxaline hydrochloride* as deliquescent prisms (12·5 g., 56%), m. p. 88—89° (decomp.). It may be recrystallised from acetone but with low recovery (Found: C, 38·2; H, 4·9; N, 12·3; S, 14·1. $C_7H_{11}O_2N_2SCl$ requires C, 37·8; H, 5·0; N, 12·6; S, 14·4%), $\lambda_{max.}$ 242 mμ (ε 8850) in H_2O. The picrate had m. p. 94—95° (decomp.) (from ethanol), Lawson and Morley [1] giving m. p. 94—96° (decomp.).

Stability of 2-Ethoxycarbonylthio-1-methylglyoxaline.—2N-Sodium hydroxide (4 ml.) was added to 2-ethoxycarbonylthio-1-methylglyoxaline hydrochloride (1 g.) in water (5 ml.) and the oil which separated extracted with ether. The dried ($MgSO_4$) ethereal solution was kept at room temperature for 17 hr. Hydrogen chloride was then passed in until precipitation was complete. The oily precipitate was extracted with water. Addition of aqueous picric acid gave 2-ethoxycarbonylthio-1-methylglyoxaline picrate (540 mg., 30%), m. p. and mixed m. p. 94—95° (decomp.).

2-Ethylthio-1-methylglyoxaline (II; R = Et).—This *compound* was prepared by Marckwald's method [2] as a colourless oil, b. p. 115—116°/18 mm. (Found: C, 50·9; H, 7·3; N, 19·6. $C_6H_{10}N_2S$ requires C, 50·7; H, 7·1; N, 19·7%), $\lambda_{max.}$ 221 (ε 6950) and 248 mμ (ε 4740) in EtOH. Its picrate had m. p. 112° (from ethanol).

1-Ethyl-2-ethylthio-3-methylglyoxalinium Iodide (IV; R = Et, X = I).—Ethyl iodide (2·9 ml., 0·036 mol.) was added to 2-ethylthio-1-methylglyoxaline (4·7 g., 0·033 mol.) in acetone (20 ml.) and kept overnight. The crystals which separated were recrystallised from acetone–ethyl acetate to constant m. p., giving the *glyoxalinium iodide* (1·8 g.), m. p. 156° (Found: C, 31·6; H, 4·8; N, 9·4. $C_8H_{15}N_2SI$ requires C, 32·2; H, 5·1; N, 9·4%). Addition of ethyl acetate to the reaction mother-liquors gave a mixture of iodides (2·4 g.), m. p. 110°, which could not be separated by crystallisation.

1-Ethyl-2 : 3-dihydro-3-methyl-2-thioglyoxaline (III; R = Et).—1-Ethyl-2-ethylthio-3-methylglyoxalinium iodide (1·5 g.) was heated at 180° until low-boiling products had ceased to distil; then the residue was distilled under reduced pressure. The latter distillate was taken up in ether, washed with 2N-hydrochloric acid and saturated sodium hydrogen carbonate solution, and dried ($MgSO_4$). Distillation of the solution gave *1-ethyl-2 : 3-dihydro-3-methyl-2-thioglyoxaline* (350 mg.), m. p. 51°, b. p. 166°/14 mm., $\lambda_{max.}$ 260 mμ (ε 14·800) in EtOH (Found: C, 50·9; H, 7·2; N, 19·4. $C_6H_{10}N_2S$ requires C, 50·7; H, 7·1; N, 19·7%). It gave a deep blue colour with Grote's reagent.[5] No picrate could be obtained. With ethyl iodide in acetone, 1-ethyl-2-ethylthio-3-methylglyoxalinium iodide was re-formed, m. p. and mixed m. p. 156°.

If the lower-melting mixture of iodides is used, an unidentified substance, m. p. 152°, sparingly soluble in ether, distils with the thioglyoxaline. It is removed by washing with hydrochloric acid, and pure thioglyoxaline is finally obtained.

Rearrangement of 2-Ethoxycarbonylthio-1-methylglyoxaline (II; R = CO_2Et).—The dried ($MgSO_4$) solution of 2-ethoxycarbonylthio-1-methylglyoxaline obtained by reaction of the hydrochloride (4 g.) with 2N-sodium hydroxide and extraction with ether (60 ml.) was divided into four equal parts and treated as follows: (*a*) Ethyl chloroformate (1 drop) was added. A little oil separated immediately and after 10 min. crystals began to separate. These were collected after 2 hr. and on recrystallisation from acetone gave 1-ethoxycarbonyl-2 : 3-dihydro-3-methyl-2-thioglyoxaline (470 mg., 56%), m. p. and mixed m. p. 123°. (*b*) Pyridine hydrochloride (*ca.* 1 mg.) was added. The effect was as recorded in (*a*) but 15 hr. were required before the separation of crystals appeared to be complete. (*c*) Pyridine (1 drop) was added. The thioglyoxaline (10 mg.) separated after 4 days. (*d*) Untreated. A trace of the thioglyoxaline separated after 3 weeks.

In a similar experiment, with the hydrochlorides of dimethylamine, aniline, and quinoline as catalysts, the separation of the thioglyoxaline was apparently complete after 4 days. With 2-ethoxycarbonylthio-1-methylglyoxaline hydrochloride as catalyst, separation was complete after 7 days. Ammonium chloride was ineffective.

[5] Grote, *J. Biol. Chem.*, 1931, **93**, 25.

XUM

Decarboxylation of Ethyl Chloroformate.—1-Ethoxycarbonyl-2 : 3-dihydro-3-methyl-2-thioglyoxaline (1 g.) in ethyl chloroformate (10 ml.) was heated at 65—70° until evolution of gases had ceased. The residue consisted of unchanged material, m. p. and mixed m. p. 123°.

Decarboxylation of 1-Ethoxycarbonyl-2 : 3-dihydro-3-methyl-2-thioglyoxaline.—This thioglyoxaline (70 g.) was heated at 150—160° until evolution of carbon dioxide had ceased (2 hr.). Fractionation of the residue yielded an oil (32·5 g.), b. p. 116—118°/17 mm. (which gave 2-ethylthio-1-methylglyoxaline picrate, m. p. and mixed m. p. 112°), and 1-ethyl-2 : 3-dihydro-3-methyl-2-thioglyoxaline (9·6 g.), m. p. and mixed m. p. 51°, b. p. 172—174/17 mm., giving with ethyl iodide 1-ethyl-2-ethylthio-3-methylglyoxalinium iodide, m. p. and mixed m. p. 156°.

Decarboxylation of 2-Ethoxycarbonylthio-1-methylglyoxaline Hydrochloride.—2-Ethoxycarbonylthio-1-methylglyoxaline hydrochloride (2 g.) was heated at 80—90° until evolution of carbon dioxide ceased, then at 130° for a further 30 min. The residue was separated into neutral and basic fractions with 2N-hydrochloric acid. The neutral fraction was an oil (10 mg.) which gave no colour with Grote's reagent. The basic fraction was an oil (350 mg.) which gave 2-ethylthio-1-methylglyoxaline picrate, m. p. and mixed m. p. 112°.

The author thanks Professor R. D. Haworth, F.R.S., and Dr. P. G. Marshall for their interest and advice.

British Schering Research Institute,
Alderley Edge, Cheshire. [*Received, February 11th,* 1958.]

---

477. *The Preparation and Analytical Properties of* NN-*Di(carboxymethyl)aminomethyl Derivatives of Some Hydroxyanthraquinones.*

By R. Belcher, M. A. Leonard, and T. S. West.

NN-Di(carboxymethyl)aminomethyl derivatives of some hydroxyanthraquinones are prepared by a Mannich-type condensation between the parent material, formaldehyde, and iminodiacetic acid. The monosubstituted derivatives prepared from alizarin and Alizarin Bordeaux R are particularly useful as indicators in complexometric titration, especially the ethylenediaminetetra-acetate titration of Pb^{2+}, Zn^{2+}, Co^{2+}, and In^{3+} in acid solution. The pH limits have been established and the interference of various ions has been examined. The indicators are stable in solution for several months. These substances also show promise as possible colorimetric reagents for Th^{4+} and Ce^{3+}.

Introduction of the strongly chelating methylamine-*NN*-diacetic acid group, $-CH_2{\cdot}N(CH_2{\cdot}CO_2H)_2$, frequently converts pH-sensitive dyes into indicators suitable for complexometric titration with ethylenediaminetetra-acetic acid.[1] Since many hydroxyanthraquinones show colour changes with pH in both acid and alkaline solution the preparation of complexometric indicators based on these substances was attempted. Accordingly, the *NN*-di(carboxymethyl)aminomethyl derivatives of 1 : 2-dihydroxy-,* 1 : 2 : 5-,* 1 : 2 : 6-, and 1 : 2 : 7-trihydroxy-, and 1 : 2 : 5 : 8-tetrahydroxy-anthraquinone have been prepared.

The preparative method was a Mannich condensation of the hydroxyanthraquinone with formaldehyde and iminodiacetic acid. An excess of the aldehyde and acid was used, but in all cases only a monosubstituted product was obtained; the dicarboxymethylaminomethyl group is assumed to be in position 3 because the reaction tends to occur in positions *ortho* to the hydroxyl groups in aromatic systems.

* Trivial names for these compounds would be alizarin complexone and Alizarin Bordeaux complexone, respectively.

[1] Anderegg, Flaschka, Sallmann, and Schwarzenbach, *Helv. Chim. Acta*, 1954, **37**, 113; Diehl and Ellingboe, *Analyt. Chem.*, 1956, **28**, 882; Tucker, *Analyst*, 1957, **82**, 284; Körbl and Přibil, *Chem. and Ind.*, 1957, 233; *Chemist Analyst*, 1956, **45**, 102.

XUM

Very little nitrogenous product was obtained from the corresponding reaction with 2-hydroxy-, 1 : 4-, 1 : 5-, or 1 : 8-dihydroxy-, or 1 : 2 : 3- or 1 : 2 : 4-trihydroxy-anthraquinone or with a mixture of the 5- and 8-sulphonic acids derived from 1 : 2-dihydroxyanthraquinone.

The free acids are yellow or orange-brown powders which in dilute solution are yellow or yellow-pink below pH 4·5, red at *ca.* pH 7, with transition to violet at higher pH's. These substances are also less soluble in ether and alcohol than the starting materials but are more soluble in water.

Analytical Reactions.—Those cations which give coloured compounds with the starting materials still react in a similar fashion with the new derivatives, but in addition several ions which show no colour reaction with the parent substance now form red chelates at pH 4·5. Thus 1 : 2-dihydroxyanthraquinon-3-ylmethylamine-*NN*-diacetic acid (*A*) reacts with ions such as Co^{2+}, Ni^{2+}, Pb^{2+}, Zn^{2+}, La^{3+}, Hg^{2+}, and Cu^{2+}. The indicator itself is red at pH 7—10, mauve at pH 11·5, and violet at pH 12·5 and if added to a solution of any of the above-mentioned ions (pH <12·5) it assumes the colour characteristic of it in the next higher pH range, *i.e.*, at pH 4·5 it changes to red, at pH 7—10 it changes to mauve, etc. Thus ions which show little tendency to form chelates in acid solution but react in alkaline solution also produce colour reactions; *e.g.*, Ca^{2+}, Ba^{2+}, Sr^{2+}, and Cd^{2+} give rise to mauve chelates at pH 10—11.

Indicator Properties.—Only the analytical reactions of acid (*A*) are described in this paper. The other compounds behave similarly. The most obvious application of these compounds lies in their potentialities as complexometric indicators. At pH 4·3 good reversible red to yellow end-points were obtained with acid (*A*) in the EDTA titration of Co^{2+}, Pb^{2+}, and Zn^{2+}. Cu^{2+} was titrated satisfactorily in solutions where its concentration was not very high; in more concentrated solution the intensely blue chelate with EDTA masked the colour change. Ni^{2+} and La^{3+} formed chelates which were sufficiently stable even in boiling solution to offer serious resistance to the action of slight excesses of EDTA. The titration of Pb^{2+} and Zn^{2+} was carried out at room temperature, but the Co^{2+} end-point is best observed at 70—80°. These titrimetric procedures are reproducible within 0·1—0·2%. Indium can also be titrated at 70—80° and pH 4, but a better end-point is obtained with 1 : 2 : 5-trihydroxyanthraquinon-3-ylmethylamine-*NN*-diacetic acid.

Comparison with Other Indicators.—Xylenol Orange which is perhaps the best complexometric indicator hitherto proposed for the titration of Pb^{2+}, Zn^{2+}, and Co^{2+} in acid solution was compared with our acid (*A*). At pH 5—6 the former gave a better colour response but the latter was preferred in more acid solution (pH 4·3—3·8). Hence use of acid (*A*) may be of advantage when it is necessary to titrate these ions in solutions of lower pH where, of course, fewer other ions interfere with the titration.

In titrations with acid (*A*) the yellow to red end-point is improved considerably by screening with Xylene Cyanol FF, a red to green end-point being obtained.

Interferences.—Small amounts of alkaline earths, Mg^{2+}, As^{3+}, Ag^{+}, Be^{2+}, or Cr^{3+} did not cause interference (when up to 5% of them was present). On the other hand Al^{3+}, Fe^{3+}, Sn^{2+}, Sn^{4+}, Ce^{3+}, Ni^{2+}, Mn^{2+}, La^{3+}, Sc^{3+}, Th^{4+}, Zr^{4+}, U^{4+}, and U^{6+} interfered seriously with the colour change. Cu^{2+}, Cd^{2+}, and Bi^{3+} did not unduly affect the quality of the end-point, but added on to the titration for the ion being determined.

Acid (*A*) can also be used as an indicator for the titration of Ca^{2+}, Ba^{2+}, Cd^{2+}, etc., in alkaline solution but the end-points offer no advantage over those of the many complexometric indicators already available for these ions.

The indicator solutions prepared as described below were stable for several months.

Acid (*A*) may also have applications as a colorimetric reagent for Ce^{3+}, Th^{4+}, etc., since the chelate compounds formed have an intense colour which is not affected by fluoride and EDTA to the same extent as the Alizarin S chelates which are completely broken down by these ions.

XUM

Experimental

Preparation of 1 : 2-*Dihydroxyanthraquinon-3-ylmethylamine*-NN-*diacetic Acid.*—Alizarin (16 g., 1 mol.) and iminodiacetic acid (22·5 g., 2·5 mol.), suspended in water (30 ml.), were treated with sodium hydroxide (13·5 g., 5 mol.) in water (60 ml.), followed by 37% formaldehyde solution (10 ml.). The mixture was diluted to 230 ml. with water, then kept at 75°, with constant stirring. A further 7 ml. of 37% aqueous formaldehyde were added after 4 hr., bringing the total amount to 3 mol. After a total reaction time of 14 hr., the mixture was diluted to 750 ml. and treated at 45° with 5N-hydrochloric acid dropwise till no more *compound* was precipitated. The precipitate was filtered off, and dissolved in distilled water (500 ml.) by adding the minimum amount of 2N-sodium hydroxide. Reprecipitation was effected at 45° by means of 5N-hydrochloric acid. After 2 hr. the precipitate was filtered off, washed with water containing a small amount of hydrochloric acid, then with a little 1 : 1-ethanol–ether. The resulting acid cake was dispersed in water (1 l.) lightly buffered at pH 5 (0·8 ml. of acetic acid and 6 g. of sodium acetate trihydrate), treated with a little charcoal at 45° for 2 hr., and filtered through paper pulp. The filtrate was extracted with ether to remove traces of alizarin) acidified with 5N-hydrochloric acid (to precipitate the pure acid) and set aside overnight, after which the precipitate was filtered off, washed as before with ethanol–ether, and dried on a vacuum hot-plate at 70° over P_2O_5. The yield was 13% and the m. p. 180° (decomp.) (Found: C, 59·2; H, 4·5; N, 3·5. $C_{19}H_{15}O_8N$ requires C, 59·2; H, 3·9; N, 3·7%).

The other compounds were prepared similarly, except that for the derivative from 1 : 2 : 7-trihydroxyanthraquinone a reaction time of *ca.* 3 hr. was preferable.

1 : 2 : 5-*Trihydroxyanthraquinon-3-ylmethylamine*-NN-*diacetic acid* (Found: C, 57·1; H, 3·7; N, 3·5. $C_{19}H_{15}O_9N$ requires C, 56·9; H, 3·7; N, 3·5%) had m. p. 203° (decomp.).

1 : 2 : 6-*Trihydroxyanthraquinon-3-ylmethylamine*-NN-*diacetic acid* (Found: C, 56·9; H, 3·75; N, 3·7%) had m. p. 200° (decomp.).

1 : 2 : 7-Trihydroxy- (Found: C, 54·4, H, 4·1; N, 3·6%), decomp. 184°, and 1 : 2 : 5 : 8-tetrahydroxy-anthraquinon-3-ylmethylamine-*NN*-diacetic acid (Found: C, 56·8; H, 3·75; N, 3·5. Calc. for $C_{19}H_{15}O_{10}N$: C, 54·6; H, 3·6; N, 3·4%), m. p. indefinite, were also prepared but were difficult to purify; since they had no unusual indicator properties, further purification was not attempted.

Reagents Required.—0·02M-*EDTA solution.* This was prepared by dissolving disodium ethylenediaminetetra-acetate dihydrate (7·45 g.) in distilled water (1 l.) and standardised both against a standard calcium solution (prepared from calcium carbonate) with murexide as indicator, and against a standard magnesium solution (prepared from pure magnesium) with Solochrome Black T as indicator.

0·01M-*Cobalt solution.* This was prepared from " AnalaR " cobalt sulphate and standardised against EDTA solution at pH 8 with Catechol Violet as indicator.

0·02M-*Zinc and lead solutions.* These were prepared from " AnalaR " lead nitrate and zinc sulphate severally and standardised against EDTA solution at pH 10 with Solochrome Black T as indicator.

0·02M-*Indium solution.* This was prepared by dissolving metallic indium (2·3 g.) in a two-fold excess of concentrated hydrochloric acid and diluting to 1 l. It was standardised by addition of an excess of 0·02M-EDTA and back-titration at pH 10, with a manganese solution at pH 10 (Solochrome Black T indicator).

Indicator solutions. 0·5% Solutions of the 3-di(carboxymethyl)aminomethyl derivatives of 1 : 2-di- and 1 : 2 : 5-tri-hydroxyanthraquinone were prepared by adding two drops of concentrated ammonia to the powder, followed by 7—8 drops of 20% ammonium acetate solution and dilution to the requisite volume.

Xylene Cyanol FF. This was a 0·1% solution in water.

Buffer solutions. (i) pH 4·3. Sodium acetate trihydrate (105 g.) and glacial acetic acid (100 ml.) were diluted to 1 l. with distilled water. (ii) pH 4—4·1. Sodium acetate trihydrate (70 g.) and glacial acetic acid (120 ml.) were diluted to 1 l. with distilled water.

Titration of Lead and Zinc.—25 ml. of either solution were treated with 3 ml. of pH 4·3 buffer (3 ml.) and a solution of acid (*A*) (5 drops), and titrated with 0·02M-EDTA to the red through pink to pure yellow end-point. The equivalence point coincides with the disappearance of the last trace of pink. The red to green end-point of the screened indicator is obtained as above, but with the addition of 2—3 drops of 0·1% Xylene Cyanol FF solution.

XUM

Titration of Cobalt and Indium.—25 ml. of 0·01M-cobalt sulphate or of 0·02M-indium solution was treated with a solution of acid (*A*) (5 drops), 0·1% solution of Xylene Cyanol FF (3 drops), and buffer of pH 4—4·1 (3 ml.), heated to 80°, and titrated with 0·02M-EDTA to the red through grey to green end-point. Because of the colour of the cobalt–EDTA complex the maximum permissible concentration limit is *ca.* 21 mg. of Co^{2+} per 100 ml. Because of this colour, the normal bright green of the screened end-point is replaced by a dull green shade in cobalt titrations.

We thank the D.S.I.R. for a grant.

DEPARTMENT OF CHEMISTRY,
THE UNIVERSITY, BIRMINGHAM, 15. [*Received, November 26th*, 1957.]

---

478. *Submicro-methods for the Analysis of Organic Compounds. Part III.* Determination of* N-*Methyl groups and the Simultaneous Determination of Alkoxyl and* N-*Methyl groups.*

By R. BELCHER, M. K. BHATTY, and T. S. WEST.

N-Methyl groups can be determined with an absolute accuracy of ±0·3% on 50-μg. samples by modification of Herzig and Meyer's method. Methoxyl and *N*-methyl groups can also be determined simultaneously on the same sample with equal accuracy by a slight modification of the procedure.

N-METHYL groups are always determined on the micro-scale by some form of the method originated by Herzig and Meyer.[1] Although the accuracy of the method is inferior to that of most other micro-methods, no alternative approach has yet been advanced. Hence an adaptation of the conventional Herzig–Meyer method was examined on the submicro-scale. Several forms of the usual apparatus were examined and a number of factors which affected results investigated.[2]

One of the major difficulties encountered in the adaptation of Herzig and Meyer's method to the sub-micro-scale was that very high blanks were obtained. This method, as opposed to the alkoxyl method, required the drastic steps of distillation of the hydriodic acid and pyrolysis of the quaternary ammonium salt (at 300—360°), so the method is subject to errors not found in the Zeisel method which it otherwise so closely resembles. High blanks were obtained because (*a*) the hydriodic acid formed an aerosol, (*b*) the vapour-laden gas stream was incompletely washed, and (*c*) the apparatus was not uniformly heated.

Aerosol formation was prevented by passing the hot gas stream from the decomposition flask over hydriodic acid boiling in a flask fitted with a water condenser. Modifications of the apparatus of Pregl and Lieb [3] and of Friedrich [4] were unsuitable but a modification of Steyermark's apparatus [5] was adopted. A second digestion flask, attached to the existing submicro-alkoxyl apparatus,[6] was used for digestion of the sample and for pyrolysing the salt, while the flask with the reflux condenser was used for collecting and boiling the distilled acid. The blanks were thus reduced to 20—30 μl. of 0·01N-sodium thiosulphate. A wide variation in the blank values obtained from successive determination was, however, still obtained.

It was suspected that these high values were caused by some hydriodic acid vapour

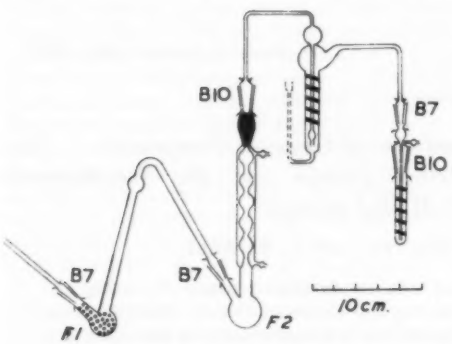
* Part II, *J.*, 1957, 4480.

[1] Herzig and Meyer, *Monatsh.*, 1894, **15**, 613; 1895, **16**, 599; 1897, **18**, 379.
[2] Bhatty, Ph.D. Thesis, Birmingham University, 1957.
[3] Pregl, "Quantitative Organic Microanalysis," 5th English Edn., J. and A. Churchill Ltd., London, 1951, p. 196.
[4] Friedrich, *Mikrochem.*, 1929, **7**, 195.
[5] Steyermark, "Quantitative Organic Microanalysis," The Blakiston Co., New York, 1951, p. 234.
[6] Belcher, Bhatty, and West, *J.*, 1957, 4480.

XUM

passing through the spiral wash-chamber. A second internal scrubbing device was therefore incorporated in the apparatus. The gas stream, before entering the spiral washer, was intimately scrubbed in a silica-wool plug which had been soaked with the wash liquid and inserted in the neck of the condenser; such a washer was used to keep down the dead-space of the apparatus.

A further source of variation in blanks was traced to irregular heating of the apparatus. The conventional copper oxide bath was, therefore, replaced by an electrically-heated aluminium block for the pyrolysis flask and another block (flame-heated) for the reflux flask.



When these measures were adopted and a carefully regulated stream of nitrogen was passed through the apparatus, the blank titres in a determination became reproducible at 15 μl. of 0·01N-thiosulphate solution. The bulk of the blank value was obtained generally in the first pyrolysis, whereas the subsequent distillations and decompositions gave negligible values.

Care was taken to ensure that the quaternary salt was decomposed below 300°, but in order to decompose the salt adhering to the outlet tube from the pyrolysis flask, the temperature was raised to 360° after the main treatment. Longer periods were used to ensure complete cleavage of the methyl iodide from the quaternary salt.

Once conditions for low and consistent blanks had been established, determinations were carried out with atropine as a reference standard. Several forms of hydrolysis flask were examined, and that adopted finally is depicted in the Figure. This hydrolysis flask has a condenser tube of the same proportions as the normal micro-apparatus.

In the initial tests recoveries were only about 50% even after three distillations and pyrolyses. Further distillation showed no significant increase in recovery, but when the pyrolysis flask was packed with glass beads (which simultaneously increased the surface area of the liquid and helped to maintain a uniform temperature inside the flask) recoveries were improved. These values are recorded in Tables 1 and 2.

It will be seen from Table 1 that the results obtained for the determination of methylimino-groups are accurate to ±0·3% except in the case of one compound, *viz.*, *N*-methyl-

TABLE 1. *Determination of N-methyl group.*

	N-Me (%)				*N*-Me (%)		
Compound	Calc.	Found	Difference (%)	Compound	Calc.	Found	Difference (%)
Atropine ...	5·19	5·14	−0·05	Ephedrine, ½H_2O	8·62	8·39	−0·23
		4·97	−0·22			8·32	−0·30
		4·97	−0·22	*iso*Quinoline methiodide	5·53	5·42	−0·11
		4·89	−0·30			5·34	−0·19
		5·02	−0·17	* *N*-Methylacetanilide	10·07	9·70	−0·37
Morphine ...	5·26	5·38	+0·12			9·52	−0·55
		5·09	−0·17			9·82	−0·25

* Low results on this compound are attributed to its volatile nature. Modification of the apparatus to include a longer air condenser between the flask *F*1 and the rest of the apparatus might yield quantitative recoveries.

acetanilide. Table 2 summarises the results obtained in the combined determination of *O*-methyl and *N*-methyl groups in the same compound. It will be seen that, even in the simultaneous determination of both groups, the accuracy is within ±0·3% in both cases. All these results were obtained on sample weights within the range 49—64 μg.

Low values for the group in *N*-methylacetanilide are attributed to the low melting point and low initial reactivity of this substance towards hydriodic acid, as some of it may be lost by volatilisation when the temperature is raised for distillation and pyrolysis.

TABLE 2. *Determination of* N-*methyl and methoxyl groups.*

	N-Me (%)			OMe (%)		
Compound	Calc.	Found	Difference (%)	Calc.	Found	Difference (%)
Narcotine	3·63	3·81	+0·18	22·52	22·72	+0·20
		3·48	−0·15		22·55	+0·03
		3·83	+0·2		22·76	+0·24
Codeine	5·02	4·96	−0·06	10·37	10·31	−0·06
		4·95	−0·07		10·29	−0·08
Cocaine	4·95	4·72	−0·23	10·23	10·48	+0·25
		4·66	−0·29		10·42	+0·19
		4·77	0·18		10·45	+0·22

Despite the reduction in weight of sample, the total time needed may exceed that required for the micro-determination. Under our conditions it is advisable to adhere to the recommended time schedule. Further modification of the apparatus might enable total time to be reduced.

EXPERIMENTAL

Reagents.—Most of the reagents were as already described;[5] the following were also required: (1) ammonium iodide, reagent grade; (2) gold chloride, 2% solution; (3) glass beads (2—3 mm. diam.) used for packing the decomposition flask, *F*1; (4) silica wool.

Apparatus.—An electrically heated aluminium block carried the decomposition flask *F*1 which was heated to 360°, while a gas-heated aluminium block supported the flask *F*2 of the alkoxyl apparatus which was heated at 150°. The apparatus is identical with that used for the determination of alkoxyl groups except that a pyrolysis flask is attached to the inlet tube.

Procedure.—A weighed [7] sample (about 50 μg.) was transferred to a platinum boat which was inserted through the B7 side arm into the flask *F*1; 20 mg. of ammonium iodide, 0·05 g. of phenol, 2 drops of gold chloride solution, and 0·5 ml. of iodine-free hydriodic acid were also added in that order. The flask was then packed with clean, dry glass beads (as indicated in the Figure) and the gas-inlet tube connected to it, silicone grease being used to seal the joint. The wash-chamber was charged with 8 ml. of a solution of sodium antimonyl tartrate, and the absorber with 1 ml. of a solution of sodium acetate in glacial acetic acid and about 0·05 ml. of bromine. The neck of the condenser was plugged with a 1·5 cm.-long wad of silica wool which had been soaked moderately with the sodium antimonyl tartrate liquid, excess being avoided.

The apparatus was assembled as indicated in the Figure. Silicone grease was used for lightly sealing all the joints except that of the absorber.

The spaces between the aluminium blocks and the flasks *F*1 and *F*2 were filled with powdered copper oxide, and thermometers placed in the oxide in contact with the flasks. A regulated stream of nitrogen (1 bubble per sec. as seen in the scrubber) was connected with the inlet tube of flask *F*1.

The following scheme was observed for heating the two metal blocks.

Time (hr.)	¼	½	1	1½	2	3
Temp. for *F*1	100°	160°	260°	300°	360°	360°
Temp. for *F*2	50	50	50	150	150	150

At the end of 3 hr., heating was discontinued and the scrubber and the absorber were disconnected.

The two flasks *F*1 and *F*2 were raised together from the heating blocks and allowed to cool to room temperature. The flow of nitrogen was then stopped. The flasks were suitably tilted so that the hydriodic acid in flask *F*2 was re-introduced into flask *F*1. Meanwhile the blocks had cooled to 160° and 50° respectively. Another absorber was attached to the scrubber and the apparatus was reassembled. The nitrogen supply was connected as before and the flasks

[7] Astbury, Belcher, and West, *Mikrochim. Acta*, 1956, 598.

XUM

were lowered into the heating blocks. The second and subsequent distillations and pyrolyses were each completed in 2½ hr., starting from the 30-min. step of the heating scheme above. Three distillations and pyrolyses for a sample and two for a blank determination sufficed to give a net titration value corresponding to the *N*-methyl content of the sample.

In the presence of methoxyl groups flasks *F*1 and *F*2 were gradually heated to 160° and 50° in 30 min. as before. These temperatures were then maintained for a further 1 hr., during which the gas stream was passed through the apparatus at the rate of one bubble per second. Methyl iodide formed from the methoxyl group was thus removed quantitatively into the absorber. Blanks were similarly determined to make allowance for the 1½ hours' digestion time. The methoxyl estimation was carried out as described previously.[4] A fresh absorber was added and the determination for *N*-methyl groups was then completed as described already, by starting from the 30-min. step in the heating scheme.

Titration of the solution containing iodine was performed in the same way as described for the alkoxyl determination.[4]

1 μl. of 0·01N-$Na_2S_2O_3$ ≡ 0·025 μg. of CH_3

CHEMISTRY DEPARTMENT, THE UNIVERSITY,
EDGBASTON, BIRMINGHAM.

[*Received, December 6th,* 1957.]

---

479. *Anionotropic Systems. Part V.* A Kinetic Investigation of the Rearrangement of 1-Phenylallyl Esters in Non-aqueous Solvents.*

By (the late) E. A. BRAUDE, D. W. TURNER, and E. S. WAIGHT.

The kinetics of the anionotropic rearrangement of 1-phenylallyl *p*-nitrobenzoate in chlorobenzene and, less extensively, acetic anhydride have been investigated. The reaction is of the first order, has a finite rate in the initial absence of acid, and is accompanied by the formation of small amounts of *p*-nitrobenzoic acid. The rate is directly proportional to the concentration of added *p*-nitrobenzoic acid. The rearrangement is intramolecular with respect to added ionic bromide but in the presence of acetic acid cinnamyl acetate is formed. 1-Phenylallyl acetate and benzoate isomerize more slowly in chlorobenzene than the *p*-nitrobenzoate and the ease of migration of leaving groups is shown to be: hydroxyl < acetate < benzoate < *p*-nitrobenzoate ≪ chloride.

A technique is described for the determination of small amounts of water in chlorobenzene.

THE rearrangement of 1-phenylallyl *p*-nitrobenzoate, $CH_2{:}CH{\cdot}CHPhX$ (X = $O{\cdot}CO{\cdot}C_6H_4{\cdot}NO_2$), to *trans*-cinnamyl *p*-nitrobenzoate, $Ph{\cdot}CH{:}CH{\cdot}CH_2X$, has played a prominent part in the development of the theory of anionotropy. The reaction was first investigated by Burton [1] and by Meisenheimer and Schmidt,[2] and more recently has been re-examined by Catchpole and Hughes.[3] Our interest in it arose from a kinetic study [4] of the acid-catalyzed isomerization of allylic alcohols.

The reaction proceeds essentially to completion and since the two isomers have considerably different light absorption at 2535 Å the system is suitable for application of the spectrokinetic method previously used.[4] Previous workers used a wide variety of organic solvents, but we have found only chlorobenzene to satisfy the necessary requirements of non-reactivity, thermal stability, and reasonable transparency to light of the appropriate

* Part IV, *J.*, 1953, 3138.

[1] Burton, *J.*, 1928, 1650; 1934, 1268.
[2] Meisenheimer and Schmidt, *Annalen*, 1933, **501**, 131.
[3] Catchpole and Hughes, *J.*, 1948, 1.
[4] Braude and Jones, *J.*, 1944, 436 *et seq.*; Braude, *Ann. Reports*, 1949, **46**, 114; *Quart. Rev.*, 1950, **4**, 404.

wavelength. A few runs were carried out with acetic anhydride as solvent but its reactivity rendered it unsuitable.

The reaction occurs at a reasonable rate in chlorobenzene at 130° and is kinetically of the first order with respect to ester, with an activation energy, derived from the limited data given in Table 1, of about 26 kcal./mole, confirming Meisenheimer and Schmidt's

TABLE 1. *Rearrangement of* 1-*phenylallyl* p-*nitrobenzoate in chlorobenzene containing acid. The effect of temperature.* (*Ester concn.*, 0·157 *mole/l.*).

Temp.	100°	100°	130°	130°
$[NO_2{\cdot}C_6H_4{\cdot}CO_2H]$ (mole/l.)	0·0021	0·0214	0·0032	0·0214
10^4k (min.$^{-1}$)	0·043	0·28	1·0	4·0

results.[2] The rate depends on the purity of the ester and of the solvent, and a side reaction affords *p*-nitrobenzoic acid, which can be extracted with water and estimated titrimetrically. A much larger quantity of *p*-nitrobenzoic anhydride is obtained from runs in acetic anhydride, probably produced by the reaction of the acid with the solvent. The elimination of *p*-nitrobenzoic acid, discussed below, was also noted by Meisenheimer and Schmidt, who claimed, however, that the addition of acid has little effect on the rate of rearrangement in ether although increasing it considerably in the absence of solvents. In chlorobenzene, however, addition of *p*-nitrobenzoic acid considerably increases the rate, and the first-order rate constant k is directly proportional to the acid concentration (Fig. 1). It was very difficult to obtain reproducible rate constants at acid concentrations less than 0·005M and reasonable values were only obtained by working with highly purified materials *in vacuo* to avoid, in particular, the presence of moisture and traces of acids. Under these conditions and in the initial absence of *p*-nitrobenzoic acid the rearrangement exhibits a finite rate which increases as the reaction proceeds, a consequence of the acid-producing reaction. This provides an unambiguous demonstration of a purely thermal anionotropic rearrangement of an allylic ester. Since the preliminary publication of this work [5] Goering and Silversmith [6] have shown that 5-methyl*cyclo*hex-2-enyl *p*-nitrobenzoate undergoes isomeric rearrangement, which is not catalysed by the *p*-nitrobenzoic acid produced, concurrently with solvolysis in aqueous acetone.

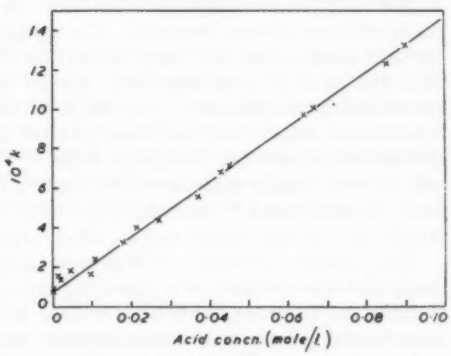


FIG. 1.

The simplest rate law fitting our results has the form:

$$\text{Rate} = k_1[\text{Ester}] + k_2[\text{Ester}][\text{Acid}]$$

i.e., the rearrangement involves a unimolecular process, $k_1 = 0{\cdot}78 \times 10^{-4}$ min.$^{-1}$, and a bimolecular process involving *p*-nitrobenzoic acid $k_2 = 1{\cdot}4 \times 10^{-2}$ l. mole^{-1} min.$^{-1}$. Further experiments designed to elucidate the precise mechanism of these two reactions are reported in the following paper.

The effect of high concentrations of foreign and common (*p*-nitrobenzoate) anions has been investigated respectively by Burton [1] and Catchpole and Hughes.[3] Burton sought to prove complete ionization of the *p*-nitrobenzoate group by showing that some cinnamyl acetate is formed when the rearrangement is carried out in the presence of acetate ions.

[5] Braude, Turner, and Waight, *Nature*, 1954, **173**, 863.
[6] Goering and Silversmith, *J. Amer. Chem. Soc.*, 1955, **77**, 6249.

He later showed that this replacement does not occur after rearrangement. Catchpole and Hughes showed that the addition of lithium *p*-nitrobenzoate causes a small increase in rate which they attributed to a salt effect, indicating that bimolecular substitution with rearrangement (S_N2') by *p*-nitrobenzoate ions is unlikely. We have confirmed these semiquantitative results by observing that in the presence of lithium *p*-nitrobenzoate (0·116M) 10^4k is about 8·8 min.$^{-1}$ in acetic anhydride at 100° compared with 3·2 min.$^{-1}$ in the absence of the salt. However, in our opinion the interpretation of Burton's experiment is equivocal in view of the well-known tenacity with which the salt used, tetramethylammonium acetate, retains water or acetic acid of crystallization.[7] Acetic acid either already present in the salt or produced by hydrolysis of the solvent (acetic anhydride) may well be an important factor since cinnamyl acetate is also produced when the ester is heated in chlorobenzene containing acetic acid. Burton's result may have been due to direct reaction of acetic acid with the ester rather than to competition between free acetate and *p*-nitrobenzoate ions for the phenylallyl cation.

In an attempt to discover the effect of added anions in the absence of large amounts of free acid the rearrangement has been carried out in chlorobenzene in the presence of di*iso*pentylammonium bromide. No cinnamyl bromide was detected in the products, the sole effect of the salt being to increase the amount of *p*-nitrobenzoic acid formed and thus the rate of rearrangement. Under these conditions the rearrangement is thus essentially intramolecular. The effect of other anions such as *p*-nitrobenzoate has not been tested since it has not been possible to find a salt which is reasonably soluble in chlorobenzene and yet thermally stable. This failure is not surprising since the cation will be only weakly stabilized by solvating chlorobenzene molecules and the salt is thus likely to decompose to uncharged products, in the case of a quaternary ammonium compound to a tertiary amine and an alkyl ester, or olefin and carboxylic acid.

The Relative Mobility of Migrating Groups in Anionotropy.—Burton and Ingold's conclusion that mobility of a migrating group in an anionotropic system increases with its stability as an anion [8] has been widely accepted although not hitherto quantitatively investigated. Some rate measurements for the anionotropy of 1-phenylallyl alcohol and its acetate and benzoate in chlorobenzene are reported in Table 2. In view of the slowness of these reactions the reasonable assumption has been made that the kinetic features of the rearrangements of the acetate and benzoate are the same as for the *p*-nitrobenzoate, namely, that essentially pure cinnamyl isomers are produced by a first-order (with respect to ester) process and that the rates are directly proportional to acid concentration. It has also been assumed that the very slow increase in intensity of light absorption at 2510 Å of 1-phenylallyl alcohol in chlorobenzene is due to the formation of cinnamyl alcohol. As is well known, the anionotropy of alcohols is dependent on catalysis by proton donors [4] or Lewis acids,[9] and in the present case the acid catalyst is derived by slight decomposition, possibly hydrolysis, of the chlorobenzene.

TABLE 2. *Rearrangements of* 1-*phenylallyl compounds in chlorobenzene at* 130°.

Compound	Concn. (mole/l.)	Acid concn. (mole/l.)	10^4k (min.$^{-1}$)
Alcohol	0·332	~0·001	~0·015
Acetate	0·089	0·015	0·038
Benzoate	0·089	0·0013	0·14
p-Nitrobenzoate	0·157	0·0036	1·0

The ease of rearrangement is in the sequence: alcohol < acetate < benzoate < *p*-nitrobenzoate, *i.e.*, the order of stability of the leaving group as an anion, as claimed by Burton and Ingold. Although different amounts of acid are eliminated from each ester, the

[7] Collie and Lawson, *J.*, 1888, **53**, 625; Willstätter and Kahn, *Ber.*, 1902, **35**, 2757; Steigmann and Hammett, *J. Amer. Chem. Soc.*, 1937, **59**, 2540.
[8] Burton and Ingold, *J.*, 1928, 904.
[9] Braude and Gore, *Nature*, 1954, **173**, 1091.

differences between the rates recorded and the calculated uncatalysed rates are, for the acetate and benzoate, negligibly small (10^4k for the isomeric rearrangement of 1-phenylallyl chloride in chlorobenzene at 100° is 50 min.$^{-1}$, about a thousand times greater than the value for the *p*-nitrobenzoate under the same conditions [10]).

The Acid-elimination.—*p*-Nitrobenzoic acid is not continuously produced during rearrangement of the ester but appears to reach a constant concentration long before the rearrangement is complete. One of us suggested that the acid may arise from a 1 : 2-elimination to give phenylallene which polymerizes to the small amount of petroleum-insoluble tar obtained in about the same yield as the acid.[4] Elemental analyses and infrared spectra now indicate that this is not the case and that the material is mainly

TABLE 3.

State of chlorobenzene	H_2O concn. (mole/l.)	Acid concn. (mole/l.)
(*a*) Saturated with H_2O	0·032	0·007
(*b*) Dried and distilled, handled in air	0·0072—0·023	0·0015—0·0026
(*c*) Dried and distilled in sealed apparatus	0·001	0·0007—0·001

cinnamyl *p*-nitrobenzoate rendered insoluble in petroleum by a very small amount of tar. The acid probably arises by hydrolysis of the ester by small amounts of water present in the solvent, a correlation between the amount of acid produced and the amount of water present being evident from the results given in Table 3. The much larger amounts of acid produced from the fused ester are clearly unlikely to arise by hydrolysis, but could result from autoxidation, since aldehydes have been reported as by-products,[2] or by ionic polymerization as suggested for the decomposition of benzyl toluene-*p*-sulphonate.[11]

EXPERIMENTAL

Light-absorptions refer to EtOH solutions.

Materials.—1-*Phenylallyl* p-*nitrobenzoate*. 1-Phenylallyl alcohol [12] (5 g.) was added to a suspension of *p*-nitrobenzoyl chloride (7 g.) in dry pyridine (10 ml.) at 0°. The mixture was kept at room temperature for 72 hr., then poured into aqueous sodium hydrogen carbonate. The ester (7·9 g., 75%) was filtered off, washed with water, and crystallized from methanol. It had m. p. 45—46° (Burton [1] gives m. p. 45—46°, Meisenheimer and Schmidt [2] give m. p. 46·2°), and $\lambda_{max.}$ 2565 Å (ε 13,800). Some specimens had slightly different m. p.s and extinction coefficients. Samples of the ester crystallized from light petroleum gave anomalous values for rate constants, apparently owing to the presence of small amounts of *p*-nitrobenzoic acid which are precipitated with the ester under these conditions but remain in solution when methanol is used as solvent.

Cinnamyl p-*nitrobenzoate*. This was prepared as above from *trans*-cinnamyl alcohol and *p*-nitrobenzoyl chloride and, crystallized from ethanol, had m. p. 77—78° (Hill and Nason [13] give m. p. 78°, Meisenheimer and Schmidt [2] give m. p. 76·5°), $\lambda_{max.}$ 2535 Å (ε 30,700).

1-*Phenylallyl acetate*. 1-Phenylallyl alcohol (20 g.), acetic anhydride (acid-free, see below) (20 g.), and pyridine were heated at 65° for 1 hr., then distilled. The acetate (15·4 g., 59%) had b. p. 82—84°/0·1 mm. (Meisenheimer and Link [14] give b. p. 110—112°/16 mm.), n_D^{20} 1·5110, $\lambda_{max.}$ 2510, 2560 Å (ε 550, 520).

Cinnamyl acetate. *trans*-Cinnamyl alcohol (10 g.), acetic anhydride (10 g.), and pyridine (9 g.) were heated at 100° for 3 hr., then distilled. The product (8·4 g., 64%) had b. p. 94—95°/1 mm., $n_D^{21·5}$ 1·5427 (Bert and Dorier [15] give b. p. 141°/18 mm., n_D^{12} 1·5442), $\lambda_{max.}$ 2500 Å (ε 17,300).

[10] Braude, Valkanas, and Waight, *Chem. and Ind.*, 1956, 314.
[11] Drahowzal and Klamann, *Monatsh.*, 1951, **82**, 460; Kochi and Hammond, *J. Amer. Chem. Soc.*, 1953, **75**, 3443.
[12] Braude and Jones, *J.*, 1946, 396.
[13] Hill and Nason, *J. Amer. Chem. Soc.*, 1924, **46**, 2236.
[14] Meisenheimer and Link, *Annalen*, 1930, **479**, 211.
[15] Bert and Dorier, *Compt. rend.*, 1930, **191**, 332.

XUM

1-*Phenylallyl benzoate.* 1-Phenylallyl alcohol (10 g.) was added to benzoyl chloride (10·5 g.) in pyridine at 0°. After 72 hr. at room temperature the mixture was poured into aqueous sodium hydrogen carbonate, and the benzoate extracted with ether. The ethereal solution was washed with water, dried (Na_2SO_4), and distilled. The ester (8·5 g., 50%) had b. p. 130—138°/0·05 mm. (Rupe and Miller [16] give b. p. 182°/12 mm.), n_D^{21} 1·5639, $\lambda_{max.}$ 2560, 2650, 2720, 2810 Å (ε 1120, 970, 970, 830).

Cinnamyl benzoate. *trans*-Cinnamyl alcohol (6·7 g.), benzoyl chloride (8 g.), and pyridine (10 g.) were kept at room temperature for 72 hr., then poured into water. The product was extracted with ether, washed with dilute hydrochloric acid and water, dried (Na_2SO_4), recovered, and distilled. The benzoate (6·8 g., 60%), b. p. 140—160°/0·005 mm. (Rupe and Miller [16] give b. p. 209°/13 mm.), solidified and, recrystallized from light petroleum (b. p. 60—80°), had m. p. 36—37°, $\lambda_{max.}$ 2465, 2510 Å (ε 21,600, 21,300).

Diisopentylammonium bromide. This was obtained by reaction of tri*iso*pentylamine and *iso*pentyl bromide at 230° (sealed tube). Recrystallized from ethyl acetate–methanol, it had m. p. 318—320° (Heilbron and Bunbury [17] give m. p. 315°).

Lithium p-*nitrobenzoate.* A solution of *p*-nitrobenzoic acid in aqueous methanol was neutralized with methanolic lithium hydroxide to Methyl Red, then evaporated slowly to dryness and dried *in vacuo*.

p-*Nitrobenzoic acid.* A commercial sample was used without further purification.

Chlorobenzene. This was kept for some time over calcium chloride and then distilled from a trace of either anhydrous potassium carbonate or sodium.

Acetic anhydride. This was kept over sodium at room temperature for 48 hr., then refluxed under reduced pressure. Distillation under reduced pressure from the mixture of sodium and sodium acetate produced yielded acetic anhydride free from acetic acid.

Kinetic Measurements.—The method of Braude and Jones [4] was modified in a few respects. As the reactions were slow the conventional oil-thermostat was replaced by a jacketed vessel, consisting essentially of a long-necked flask (A) (capacity 50 ml.), fitted with a cold-finger, sealed into a 1 l. flask (B) provided with a reflux condenser. A suitable liquid was boiled in flask (B) by means of an electrical heating mantle. *iso*Pentyl alcohol and water were used as the heating liquids for runs at 130° and 100° respectively, care being taken to avoid overheating by ensuring that the flask (A) was not immersed in the heating liquid itself. *p*-Nitrobenzoic acid, accurately weighed, was placed in the flask (A), which was heated to the appropriate temperature. A weighed amount of 1-phenylallyl *p*-nitrobenzoate was dissolved in the correct volume of solvent (usually 25 ml.) and poured into flask (A). After 10 min., when all the acid had dissolved and the solution had reached the correct temperature, a 1 ml. sample was withdrawn by inserting a long narrow-stem pipette through the neck of the flask (A) after temporary removal of the cold-finger, and the time noted. The sample was diluted with ethanol, the pipette was washed with ethanol, and the solution and washings were made up to 50 ml. The intensity of light absorption at 2535 Å of the solution was measured on a Beckman spectrophotometer (model DU). Further samples were taken at appropriate intervals. When acetic anhydride was used as solvent samples were diluted into chloroform. In runs involving the liquid 1-phenylallyl esters the above procedure was altered. The weighed ester, contained in a short specimen tube, was dropped into the solvent already heated to the correct temperature. The apparatus was shaken vigorously and the first sample taken immediately.

First-order rate constants are calculated from the expression,

$$k = (2{\cdot}3/t) \log_{10}[(a - x_0)/(a - x)],$$

where k is the rate constant (min.$^{-1}$), t is the time (min.), a is the final intensity, x_0 the initial intensity, and x the intensity of light absorption at time t.

In the runs tabulated the light absorption of the solvent has been subtracted from extinction coefficients given. In very slow runs the reaction was not followed to completion and the values taken for a (marked with an asterisk) assume complete rearrangement to the cinnamyl compound. Concentrations are corrected for solvent expansion.

Rearrangement of 1-*Phenylallyl* p-*Nitrobenzoate under Conditions of High Purity.*—Ten Pyrex ampoules were each charged with 54·8 mg. of the ester, and sealed on to the apparatus

[16] Rupe and Miller, *Helv. Chim. Acta*, 1921, **4**, 841.
[17] Heilbron and Bunbury (Eds.), "Dictionary of Organic Compounds," Eyre and Spottiswoode, London, 1953.

as shown in Fig. 2. A thick ampoule containing potassium hydroxide (100 mg.) was sealed on as at *B*, and all air in the apparatus displaced by nitrogen.

Rearrangement of 1-*phenylallyl* p-*nitrobenzoate in chlorobenzene*, 130°. *Ester concn.*, 0·157 *mole/l.* p-*Nitrobenzoic acid concn.*, 0·0107 *mole/l.*

t (min.)	0	690	1380	2820	4270	5705	10,010	
$E^{1\%}_{1\text{ cm.}}$	480	567	633	734	854	895	1040	
10^4k (min.$^{-1}$)	—	2·44	2·31	2·14	2·58	2·35	—	(mean 2·4)

Rearrangement of 1-*phenylallyl acetate in chlorobenzene*, 130°. *Ester concn.*, 0·089 *mole/l.*

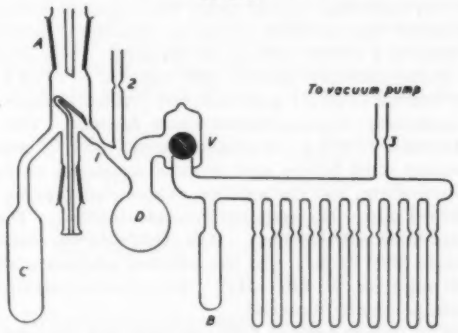
t (min.)	0	15,865	30,450	78,100	148,100	—	
$E^{1\%}_{1\text{ cm.}}$	52	102	157	286	455	960 *	
10^4k (min.$^{-1}$)	—	0·035	0·040	0·038	0·040	—	(mean 0·038)

Rearrangement of 1-*phenylallyl benzoate in chlorobenzene*, 130°. *Ester concn.*, 0·089 *mole/l.*

t (min.)	0	5775	9810	15,575	24,200	38,600	—	
$E^{1\%}_{1\text{ cm.}}$	93	156	181	225	315	394	820 *	
10^4k (min.$^{-1}$)	—	0·16	0·13	0·13	0·15	0·14	—	(mean 0·14)

Meanwhile purified chlorobenzene (100 g.) had been refluxing gently with sodium (1 g.) in a flask to which was attached a fractionating column (18 in., Fenske-ring packed) and vacuum take-off head delivering into the apparatus at *A*. After 24 hr. the rate of heating was increased

FIG. 2.



until distillation commenced. The first fraction (20 ml.) was rejected into *C* and the next (50 ml.) collected in *D*. The tubes at the points of sealing 1 and 2 were swept with nitrogen to remove any chlorobenzene and sealed. The chlorobenzene was then frozen and the apparatus evacuated. After several alternate meltings of the chlorobenzene and evacuation, the apparatus was sealed off at 3 with as hard a vacuum as could be obtained (about 2×10^{-3} mm. Hg) with the potassium hydroxide molten and the magnetic valve *V* (a ball bearing on a ground-glass seating) held open. After the chlorobenzene had warmed to room temperature one ml. was distilled into each ampoule in turn by cooling with liquid nitrogen and the ampoule sealed off. In order to prevent pyrolysis of the solvent vapour at the seal, the valve *V* was closed during the operation of sealing, and the ampoule kept at liquid-nitrogen temperature. After being heated at 130° for various times, the ampoules were cooled in ice and opened, and 0·04 ml. was removed by a micrometer syringe. This was diluted with ethanol for spectrometric analysis. The remaining 0·96 ml. was titrated in water with alkali by the cathode-ray polarographic procedure.

t	Acid concn. (μmole/ml.)	$E^{1\%}_{1\text{ cm.}}$	10^4k (min.$^{-1}$)	t	Acid concn. (μmole/ml.)	$E^{1\%}_{1\text{ cm.}}$	10^4k (min.$^{-1}$)
0	—	482	—	13,380	0·8	886	0·96
1725	<0·1	553	0·78	21,720	1·58	1024	—
3090	0·2	613	0·86	30,240	1·63	1040	—
6030	0·4	733	1·02	40,220	1·87	—	(mean) 0·91

Reaction Products of the Rearrangement of 1-*Phenylallyl* p-*Nitrobenzoate.*—(i) *Chlorobenzene solution.* A solution of the ester (2·5 g.) in chlorobenzene (25 ml.) was heated at 130° for 21 days. The solvent was evaporated under reduced pressure and the residue extracted with light petroleum (b. p. 60—80°), leaving an insoluble gum (150 mg.) with an infrared spectrum similar to that of cinnamyl *p*-nitrobenzoate (Found: C, 65·8; H, 5·0. Calc. for $C_{16}H_{13}O_4N$: C, 67·5; H, 4·6%). The petroleum solution was evaporated to dryness, and the solid dissolved in ether and extracted with aqueous sodium carbonate (5 × 25 ml.). The ethereal solution was dried (Na_2SO_4) and distilled, leaving a solid (2·35 g., 94%) which after crystallization had m. p. 77—78° undepressed by *trans*-cinnamyl *p*-nitrobenzoate. The light absorption max. was at 2535 Å (ε 30,700). The aqueous sodium carbonate extract was acidified with concentrated hydrochloric acid and extracted with ether (5 × 25 ml.). The ether extract was washed once with water, dried (Na_2SO_4), and distilled. The residue (17·7 mg.), crystallized from water, had m. p. 238—240°, undepressed by *p*-nitrobenzoic acid. A fresh specimen of 1-phenylallyl *p*-nitrobenzoate treated in the above manner yielded none of the acid.

(ii) *Acetic anhydride solution.* The ester (1·25 g.) in acid-free acetic anhydride (25 ml.) was heated at 100° for 17 days. The solvent was then distilled under reduced pressure. No cinnamyl acetate was obtained. The residue was extracted with light petroleum (b. p. 80—100°), leaving an insoluble solid (200 mg.), which after crystallization from ethyl acetate had m. p. 176—177°, undepressed by *p*-nitrobenzoic anhydride, prepared by refluxing *p*-nitrobenzoic acid in acetic anhydride for 65 hr. Evaporation of the petroleum extract yielded cinnamyl *p*-nitrobenzoate.

(iii) *Chlorobenzene solution containing acetic acid.* A solution of the ester (2·5 g.) and dry acetic acid (1·0 ml.) in chlorobenzene (25 ml.) was heated at 130° for 4 days. The cold solution was diluted with ether and extracted several times with aqueous sodium hydrogen carbonate solution. The aqueous layer was acidified as above, yielding *p*-nitrobenzoic acid (480 mg.) (extraction with ether yielded a further 70 mg. of the acid). The ethereal extract was dried (Na_2SO_4) and distilled, giving cinnamyl acetate (300 mg.), b. p. 72°/0·1 mm., n_D^{26} 1·5373, $\lambda_{max.}$ 2510 Å (ε 17,100). The residue (1·32 g.) was cinnamyl *p*-nitrobenzoate.

(iv) *Chlorobenzene containing diisopentylammonium bromide.* The ester (1·252 g.) and di*iso*pentylammonium bromide (1·670 g.) in chlorobenzene (50 ml.) were heated at 130° for 5 days. The solution became dark brown and crystals separated on cooling. The semisolid mass was dissolved in chloroform, and the solution evaporated, leaving a dark brown residue, which was heated at 160°/0·1 mm. No cinnamyl bromide distilled. The residue was extracted with ether, leaving the insoluble salt (850 mg.). The ether solution was extracted with aqueous sodium hydrogen carbonate (5 × 25 ml.), and the aqueous solution acidified as above, yielding *p*-nitrobenzoic acid (250 mg.), m. p. 240—241°. The ethereal solution contained cinnamyl *p*-nitrobenzoate and some polymeric material.

Assay and Separation of p-*Nitrobenzoic Acid* (*for Low and Medium Concentrations*).—The acid was detected in aqueous solution by cathode-ray polarography. The " wave " due to hydrogen-ion reduction at a platinum microelectrode was observed on a cathode-ray polarograph at a rate of potential increase of 10 v/sec. and a sweep repetition frequency of 2 per sec. At this rate of increase of potential, the wave height was insensitive to stirring of the solution, and no undue " broadening " of the wave due to slowness of reduction was found. The use of such a high rate of sweep was made feasible by capacity current compensation by a novel method.

In the region of interest, from *ca.* 0 to −0·6 v (with respect to the saturated calomel electrode used as working anode), it was found that the behaviour of the microelectrode (a 5 mm. long platinum wire of 0·001 in. diam.) in the supporting electrolyte alone (0·1N-potassium chloride) could be simulated by a capacitance and resistance in parallel. The currents resulting from the application of the sweep potential to the polarographic cell and to an equivalent RC network were subtracted electronically, leaving only the signal due to reducible ions.

Potassium hydroxide solution (0·5M) was added from a micrometer syringe to the rapidly stirred mixture of supporting electrolyte (5 ml.) and chlorobenzene solution of *p*-nitrobenzoic acid (1 ml.) until the hydrogen-ion " wave " continuously observed on the cathode-ray tube disappeared. Only at high acid concentrations was the speed of titration seriously limited by the slow establishment of partition equilibrium of the acid between the two solvents. The end-point was determined by graphical interpolation, the values of " wave height " (on an arbitrary scale) being plotted against titre. The smallest quantity of acid which could be titrated by this method was 2×10^{-7} mole, corresponding to a concentration in the aqueous

phase of 10^{-5} mole/l. Determinations were reproducible to 10^{-7} mole. The acid produced during the reaction was also determined by adding 1 ml. samples of the chlorobenzene solution to water (25 ml.) and titrating them with 0·001M-ammonia to Methylene Blue–Neutral Red used as a " flash-indicator."

Determination of Traces of Water in Chlorobenzene.—Methanol dried by magnesium turnings was distilled into a dropping funnel containing freshly dried potassium nitrate on a wad of glass wool just above the tap. The resultant anhydrous solution had sufficient electrolytic conductivity to permit its use for polarographic measurements. A suitable volume (1—5 ml.) was run directly into the polarograph cell without exposure to air, and excess of Karl Fischer reagent was added from a micrometer syringe, stirring being by dry nitrogen. Two platinum electrodes were immersed in the solution, one large and relatively unpolarisable (3 cm. long, 0·2 mm. thick), and one small (2 mm. long, 0·01 mm. thick). Application of a linearly increasing potential between the electrodes (the microelectrode becoming negative) produced an iodine diffusion peak which was observed on the cathode-ray polarograph, as described for acid assay. The iodine peak height was found to be proportional to the iodine concentration, and hence to the excess concentration of Karl Fischer reagent. Addition of a water-containing solution reduced this peak height and sufficient Karl Fischer reagent was then added to restore it to its previous value or to the appropriate new value if an appreciable volume change resulted. The Karl Fischer reagent was standardized independently by titration of a standard solution of water containing 5 mg./ml.; 0·1 ml. of the standard solution of water required 0·119 ml. of Karl Fischer reagent. Since 0·119 ml. were delivered by 595 divisions on the micrometer syringe, 1 division is equiv. to 0·84 μg. of water.

Four samples of chlorobenzene were prepared, of decreasing degrees of wetness: (*a*) Untreated chlorobenzene was shaken with distilled water for 24 hr. and separated. (*b*) Chlorobenzene was dried ($CaCl_2$) and distilled, and then left in a glass-stoppered bottle for some months. (*c*) Chlorobenzene was freshly dried ($CaCl_2$) overnight and distilled, without special precautions. (*d*) Chlorobenzene from (*c*) was redistilled from sodium directly into the polarographic cell in an apparatus sealed against moisture. Results are tabulated.

Chlorobenzene (ml.)	Karl Fischer (div.)	H_2O (10^{-6} g.)	Mean H_2O concn. (mole/l.)
(*a*) 0·03, 0·03	18·5, 19·5	15·5, 16·3	0·032
(*b*) 0·01	5	4·2	0·023
(*c*) 0·295, 0·295, 0·11, 0·15	32·6, 53, 17·8, 19·1	27·4, 44·5, 14·9, 16·1	0·0072
(*d*) 1·0, 0·5, 1·0, 1·0, 1·0	22·4, 7·35, 17·8, 10·9, 39·8	18·9, 6·15, 15·0, 9·14, 33·5	0·0010

Acid Production from 1-*Phenylallyl* p-*Nitrobenzoate in Wet Chlorobenzene.*—The ester (200 mg.) was dissolved in chlorobenzene (*a*) (4 ml.), and the solution sealed into two 2 ml. ampoules and heated at 130° (1) for 7200 min. and (2) for 23,000 min. The ampoules were cooled and the acid produced measured by polarographic titration: (1) 0·95 μmole/ml., (2) 7·0 μmole/ml.

One of us (E. S. W.) is indebted to the Department of Scientific and Industrial Research for a maintenance grant during 1948—50.

Imperial College of Science and Technology,
London, S.W.7.

[*Received, January 9th,* 1958.]

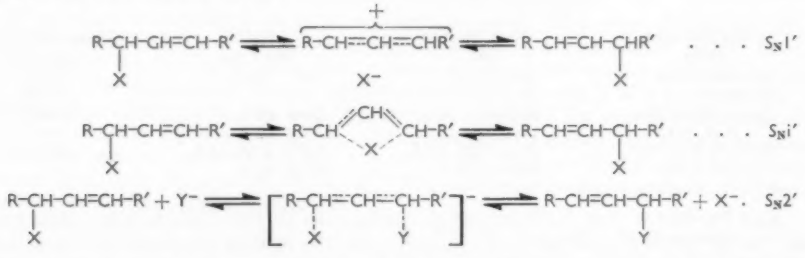
XUM

480. *Anionotropic Systems. Part VI.* The Rearrangement of 1-Phenylallyl p-Nitrobenzoate in Chlorobenzene. Tracer Studies.*

By (the late) E. A. Braude and D. W. Turner.

The isomerisation of 1-phenylallyl *p*-nitrobenzoate has been shown * to involve (i) a unimolecular process and (ii) a bimolecular reaction with *p*-nitrobenzoic acid. By use of ^{18}O as tracer the former was shown to be intramolecular, in not producing equilibration of the carboxyl-oxygen atoms. By use of *p*-nitro[*carboxy*-^{14}C]benzoic acid the bimolecular reaction was shown to involve attack by essentially undissociated acid molecules at both positions 1 and 3 in the ester, as well as catalysis of the intramolecular reaction.

Of the three principal mechanisms proposed for anionotropic rearrangement, namely, unimolecular (S_Ni'), intramolecular (S_Ni') and bimolecular (S_N2'), the last, understood as synchronous rearrangement by anions,[1] is rare, being readily observed only in systems where normal replacement (without rearrangement—S_N2) which tends to obscure it is much reduced,[2] or in isotopic exchange experiments.[3] This has been ascribed to the electrostatic repulsion between the negatively charged reagent and the double-bond π-electron system. It has been pointed out by one of us, however, that attack by a neutral reagent will not be thus hindered,[4] and examples of bimolecular rearrangement involving attack by amines are well known.[5,6] However, in the best authenticated example (involving a secondary amine) a hydrogen-bridge may be present in the transition state and such a reaction is best regarded as of the S_Ni' type.[7]



It has been shown [8] in these laboratories that rearrangement of allylic alcohols in aqueous organic media is essentially acid-catalysed and may involve bimolecular attack of a solvent molecule on the oxonium ion. Previous studies of the rearrangement of allylic esters have been carried out under conditions involving in all probability the presence of significant amounts of acids. The first indubitable demonstration of a purely thermal rearrangement of an allylic ester, described in the previous paper, required refined techniques to secure exclusion of water, acids, and oxygen. The purpose of the present paper is to describe the investigation of this thermal rearrangement by means of ^{18}O as

* Part V, preceding paper.

[1] Hughes, *Trans. Faraday Soc.*, 1938, **34**, 194.
[2] de la Mare and Vernon, *J.*, 1952, 3325, 3331, 3628.
[3] England and Hughes, *Nature*, 1951, **168**, 1002.
[4] Braude, *Ann. Reports*, 1949, **46**, 125.
[5] Young, Webb, and Goering, *J. Amer. Chem. Soc.*, 1951, **73**, 1076; Young, Clement, and Shih, *ibid.*, 1955, **77**, 3061.
[6] Stork and White, *ibid.*, 1953, **75**, 4119.
[7] Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953.
[8] Braude, Jones, and Stern, *J.*, 1946, 396; Braude, *J.*, 1948, 794; Braude and Coles, *J.*, 1951, 2085.

tracer, and of the acid-catalysed rearrangement by means of *p*-nitrobenzoic acid labelled with ^{14}C in the carboxyl position.

Experimental

p-*Nitro*[carboxy-^{14}C]*benzoic Acid*.—Potassium [^{14}C]cyanide (0·4 mc) was dissolved in distilled water (3 ml.) containing inactive potassium cyanide (61 mg.) as carrier. A solution of copper sulphate (150 mg.) in distilled water (3 ml.) was added and the solution gently boiled to expel cyanogen liberated in the decomposition of the cupric cyanide. The cyanogen (carrying half of the initial ^{14}C) was trapped in sodium hydroxide solution. The slurry of cuprous cyanide was transferred to a small Soxhlet extractor fitted with a sintered-glass disc in place of the usual thimble, filtered, and washed twice with distilled water. A 5 ml. flask was attached and the solid dried by connection to a vacuum-line. Dry air was admitted and the solid extracted by refluxing dry pyridine (3 ml.). Pure cuprous cyanide was extracted into the flask and left as yellow crystals after removal of the pyridine in a vacuum. Dry *p*-bromonitrobenzene (100 mg.) was added and fresh dry pyridine (0·25 ml.) was vacuum-distilled in from a pellet of potassium hydroxide. The mixture was heated at 180—190° under nitrogen for 22 hr., then cooled, syrupy phosphoric acid (1 ml.) and diethylene glycol diethyl ether (0·3 ml.) were added, and the whole was reheated to 160° for 1 hr. After cooling, the solid was triturated with water (2 ml.) and filtered off. *p*-Nitrobenzoic acid, isolated by repeated extraction with aqueous sodium hydroxide solution followed by acidification with hydrochloric acid, was washed with ice-cold water, crystallised twice from aqueous methanol, and dried *in vacuo* (m. p. and mixed m. p. 142°).

The combined yield from two such preparations was 58·4 mg., (29% based on total potassium cyanide used). This product was dissolved in redistilled acetone (25 ml.) to yield a stock solution. The specific activity of this solution was $1{\cdot}26 \times 10^5$ counts per min. per ml. when counted in the standard manner (see below) and the acid thus had a specific molar activity of 9000 counts per min. per 10^{-6} mole.

1-*Phenylallyl* p-*Nitro*[carbonyl-^{18}O]*benzoate*.—Water (0·44 g.) containing 9·69 atoms % of ^{18}O was added to a solution of *p*-nitrobenzoyl chloride (4·48 g.) in pyridine (10 ml.). After the initial reaction had subsided, the mixture was stirred on the steam-bath for 3 hr. in order to complete exchange between the two carboxyl-oxygen positions. Ether (8 ml.) was added to the cooled mixture, and the precipitated solids were separated on the centrifuge, washed twice with ether, and dried in a vacuum. The dry solid was added in small portions to excess of thionyl chloride boiling under reflux, and the mixture heated for 2 hr. The remaining thionyl chloride was then removed by distillation and the removal completed by addition and distillation of carbon tetrachloride (2 × 2 ml.).

The residue (9·3 g.) (mainly *p*-nitrobenzoylpyridinium chloride) was stirred into dry pyridine (10 ml.) and cooled in ice, and 1-phenylallyl alcohol (3·2 g.) was added with stirring. After 2 days at room temperature, the 1-phenylallyl *p*-nitrobenzoate was separated and purified as described in the previous paper. Material twice recrystallised from methanol (1·9 g., 28%) had m. p. 47·5°, $\lambda_{max.}$ 2595 Å (ε 14,100).

Cinnamyl *p*-nitro[^{18}O]benzoate was prepared in the same manner from cinnamyl alcohol.

Kinetic Procedure.—Runs were carried out at 130° as described in the preceding paper.

A quantity of unlabelled recrystallised *p*-nitrobenzoic acid (m. p. 140—141°) sufficient to bring the acid concentration to the desired value was weighed in a short specimen tube, an aliquot part (usually 1 ml.) of the acetone solution of labelled acid was added, and after all had dissolved the acetone was removed in a gentle stream of nitrogen. The tube and contents were dropped into chlorobenzene (25 ml.) in the heated reaction vessel, and the mixture well shaken to complete dissolution. 1-Phenylallyl *p*-nitrobenzoate (1·37 g.) in a similar specimen tube was then added and one minute of vigorous shaking was allowed for temperature equilibration. The first samples were then removed, this being taken as zero time. 1 ml. samples were removed for spectrometric assay as described in the preceding paper. 1 ml. samples were taken for exchange measurements at frequent intervals, and after about 500 min. (at *t'*) 7 ml. of solution were removed for ester radioactivity analysis.

Measurement of Radioactivity.—An internal-sample proportional counter, flushed with methane at atmospheric pressure and operated at 3000 v, was employed.

After polarographic titration of the 1 ml. samples (for details see preceding paper), the neutralised chlorobenzene and aqueous layers were allowed to separate and a 1 ml. portion of

71

XUM

the aqueous layer was removed and evaporated to dryness on a nickel-coated dish (1 in. diam.). The residue was dissolved in *NN*-dimethylformamide (0·4 ml.) by gentle swirling and its activity determined. Such a sample was of " infinite thickness " and of very reproducible surface. Under these conditions, the observed count rate was proportional to the concentration of the active material per g. of solution. A standard procedure employing 0·4 ml. of solvent was adopted, a correction being made when large quantities of solute were introduced. Activities are expressed throughout as counts per min. per mg., or counts per min. per 10^{-6} mole, it being understood that 0·4 ml. of supporting solvent was used. The solvent used for assay of esters and of the free acid was diethylene glycol diethyl ether.

At the highest acid concentrations (0·05—0·09 mole $l.^{-1}$) 1 ml. samples were removed from the reaction mixture in a pre-heated pipette (to prevent immediate crystallisation of the acid) and run into light petroleum (b. p. 40—60°; 3 ml.) contained in a centrifuge tube. The precipitated acid was centrifuged, washed three times with light petroleum, and dried. Recovery was quantitative. The acid was dissolved in the ether (0·4 ml.) and transferred to a nickel-plated dish for counting.

Separation of Mixtures of Esters.—(i) *Sublimation.* The mixture of esters, from which the solvent had been removed under vacuum, was placed in a microsublimation apparatus (distance, sample to cold finger, 1·5 cm.) and sublimed at $60°/10^{-3}$ mm. for about 1 hr. The light absorption at 2535 Å and radioactivity in diethylene glycol diethyl ether (0·4 ml.) were measured. A portion of the mixture before sublimation was also assayed for radioactivity and, since the proportion of the two isomers (α and γ) in the mixtures was known from the light-absorption data, the specific activities of the individual isomers could be determined by solving the simultaneous equations for the specific activities of the two mixtures. Test sublimation of a synthetic mixture showed that rearrangement was not appreciable under the conditions used.

(ii) *Crystallisation.* The mixture of esters was crystallised from methanol between room temperature and −15°, giving a product in which the relative proportion of isomers (obtained by measurement of light absorption at 2535 Å) was altered. The specific activity of each isomer could be determined as above.

(iii) *By chromatography* [9] (*used in* ^{18}O *studies only*). The mixture of esters (50—200 mg.) was applied in light petroleum (b. p. 40—60°) to a column of silica gel (200 mesh; 2 cm. diam. × 12 cm. long contained in a Pyrex tube) rendered fluorescent by the admixture of activated Willemite (20 mg.). The esters were eluted with light petroleum (b. p. 40—60°) containing 2% of diethyl ether. Under irradiation by ultraviolet light (from a Hanovia mercury-vapour lamp) the esters were revealed as dark bands upon the white fluorescence of the column. The relative speeds of movement of the two bands were as 5·5 (band II) : 7·5 (band I). Band I on elution, and removal of the solvent, gave 1-phenylallyl *p*-nitrobenzoate, m. p. 45°, raised to 46·5° by recrystallisation from methanol. Band II similarly gave cinnamyl *p*-nitrobenzoate m. p. 68—72°, raised to 78° by recrystallisation from ethanol. Pure 1-phenylallyl *p*-nitrobenzoate was recovered quantitatively and showed less than 2% of rearrangement after chromatography under these conditions.

Determination of Carbonyl-^{18}O *Enrichment.*—A 1% w/v solution of labelled cinnamyl *p*-nitrobenzoate in carbon tetrachloride was contained in a micrometer cell (sodium chloride windows; Research and Industrial Instruments Co.) set to a path-length of 0·85 mm. and placed in the sample beam of an infrared double-beam spectrometer (Grubb-Parsons, Model S4). A similar cell containing a solution of pure unlabelled ester of the same strength was placed in the reference beam, and the path-length was adjusted to give identical absorption at all wavelengths (except near the 6 μ carbonyl band). The only absorption then remaining was a band at 1700 $cm.^{-1}$ due to $C{=}^{18}O$. Proportionality between enrichment (in excess of the natural enrichment) and the intensity of this band was confirmed by making accurate dilutions of a sample of labelled ester with unlabelled material.

	Relative concn. of labelled ester	Optical density at 1700 $cm.^{-1}$
Before dilution	1·00	0·037
1st dilution	0·49	0·018
2nd dilution	0·24	0·009

Accuracy.—The precision of the measurements made as above was limited by the finite width of the recorder trace and by noise, together equivalent to *E ca.* 0·002.

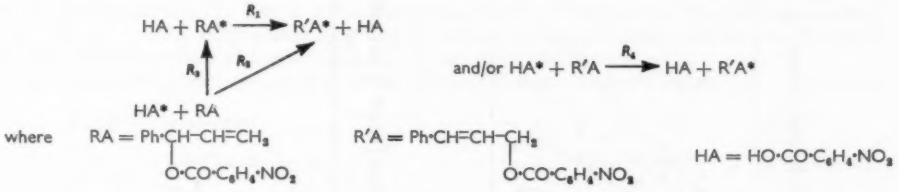
[9] Searse, *J. Amer. Chem. Soc.*, 1948, **70**, 3630.

Determination of the Molecular Weight of p-*Nitrobenzoic Acid in Chlorobenzene.*—The elevation of the b. p. of chlorobenzene on addition of *p*-nitrobenzoic acid was compared with that produced by anthracene. The boiling temperature was measured by a thermistor (resistance 2075 ohms at 132°) in one arm of a Wheatstone bridge. The b. p. elevations observed corresponded to *M* 175·0 and 175·5 at concentrations of 9·08 and 17·35 g. l.$^{-1}$ respectively (Calc. for $C_7H_5O_4N$: *M*, 167·05).

Results

^{14}C *Studies.*—The initial overall rate of exchange (R_e) of the *p*-nitrobenzoyl group between initially inactive 1-phenylallyl *p*-nitrobenzoate, and added radioactive *p*-nitrobenzoic acid in chlorobenzene at 130° was followed by measurements of the decrease in radioactivity of samples of the acid withdrawn from the reaction mixture. The relative contributions to this overall rate by exchange without rearrangement (S_N2?) at a rate referred to as R_3, and exchange with rearrangement, referred to as R_2, were deduced from the specific radioactivities of samples of the starting material and of the product of rearrangement, isolated shortly after the commencement of the reaction.

With no assumptions as to the mechanism of the individual steps, the increase of activity in α- and γ-esters was considered to arise in the manner summarised in the annexed schemes. R_1, R_2, R_3, and R_4 are the rates of formation of the various labelled products in mole l.$^{-1}$ min.$^{-1}$.



In order further to simplify the investigation, the contribution of exchange with the γ-ester was determined separately. It was negligible, the half-time of exchange between γ-ester (0·171 mole) and labelled *p*-nitrobenzoic acid (0·0096 mole) being not less than 4×10^4 min. That is, the exchange was more than 100 times slower than that with the α-ester under the same conditions. For the purpose of evaluation R_1, R_2, R_3, and, therefore, R_4 could be neglected.

Now, the specific molar activity of the γ-ester being produced at any instant was considered to be the sum of the instantaneous specific activity of the α-ester, multiplied by the fraction of ester produced by the intramolecular route, and the instantaneous specific activity of the acid, multiplied by the fraction of γ-ester produced by the bimolecular route:

$$y(\mathrm{i}) = xR_1/R_{\mathrm{obs.}} + AR_2/R_{\mathrm{obs.}}$$

Where y(i), x, and A were the instantaneous specific molar activities of the γ-ester, α-ester, and acid respectively, and $R_{\mathrm{obs.}}$ was the total rate of rearrangement.

The observed specific activity (y) of the γ-ester after a time of reaction (t') was therefore:

$$y = \bar{x}R_1/R_{\mathrm{obs.}} + \bar{A}R_2/R_{\mathrm{obs.}}$$

where $\bar{x}$ and $\bar{A}$ are the mean specific molar activities from the start of the experiment to the time of determination of y:

$$\bar{x} = \frac{1}{t'}\int_0^{t'} x\,\mathrm{d}t \qquad \bar{A} = \frac{1}{t'}\int_0^{t'} A\,\mathrm{d}t$$

Now, since $R_{\mathrm{obs.}} = R_2 + R_1$, rearrangement of the above expression for y gives:

$$R_2/R_{\mathrm{obs.}} = (y - \bar{x})/(\bar{A} - x)$$

$\bar{x}$ was determinable from x, and $\bar{A}$ from the rate of loss of activity from the acid. The evaluation of R_2 (and hence R_1) rested then on the measurement of the specific molar activities of the α-ester and γ-ester at any single time after the commencement of exchange, between such limits that the ester activities should be high enough to measure, and that the rearrangement had not proceeded so far as to alter markedly the α-ester concentration. To this end, a portion of the reaction mixture was generally removed for ester analysis when exchange was between 50% and 80% complete.

x and y were not determined directly for the pure esters, since separation of a mixture containing more than a few per cent. of γ-ester was tedious. Since, however, the proportion of each ester in a mixture was readily found by light-absorption measurements, partial separation and comparison of the specific activities before and after separation gave simultaneous equations in x and y which were readily soluble.

The partial separation required was effected by crystallisation from cold ethanol or by sublimation in a high vacuum.

FIG. 1. *The influence of* p-*nitrobenzoic acid concentration on the rates of the reactions* R_1, R_2, R_3, R_r. *The curves (from top to bottom) relate to* R_r, R_1, R_3, R_2.

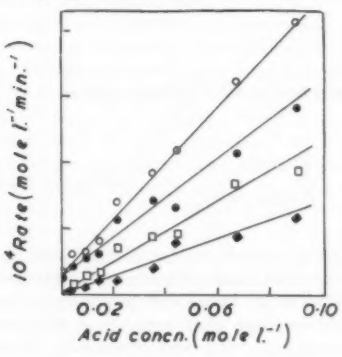
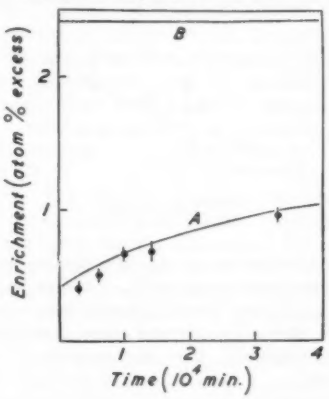


FIG. 2. *The time variation of the carbonyl-oxygen* ^{18}O *enrichment in cinnamyl* p-*nitrobenzoate. A, Calc. for Case* I *and Case* II *(see text). B, Calc. for complete oxygen equivalence during rearrangement.*



During sublimation, enrichment of α-ester in the sublimate took place, the γ-ester being much less volatile. Crystallisation produced enrichment of either α- or γ-ester depending on the proportions in which they were initially present and on the conditions of crystallisation. In all runs it was found that the two esters had specific activities of the same order of magnitude, that of the γ-ester tending to become higher than that of the α-ester by as much as four times at lower acid concentrations; this shows both α- and γ-attack by the labelled acid to take place. The difference between R_2 and the total rate of rearrangement (R_r) gave the rate of intramolecular rearrangement (S_Ni') referred to as R_1. The experimental data relating to fourteen kinetic experiments are summarised in the Table, and the derived values of R_1, R_2, and R_3 are plotted together with R_r *versus* acid concentration in Fig. 1.

^{18}O *Studies.*—The mechanism of the thermal rearrangement was investigated (at the suggestion of Dr. L. M. Jackman) by the use of ^{18}O to differentiate between the alkoxyl and carbonyl positions of the carboxylate group. The continued non-equivalence of these positions, *i.e.*, the lack of alteration of isotopic enrichment of the labelled position, can only be maintained in a carboxylate group which remains bound to the rest of the molecule throughout rearrangement. This criterion makes no distinction between a fully covalent cyclic process and the intermediate formation of a tight ion pair but may be used to detect the formation of kinetically free and mesomeric anions. Such a distinction has been obtained in an analogous case by Denny.[10]

[10] Denny, *J. Amer. Chem. Soc.*, 1955, **77**, 1706.

The isotopic enrichment (meaning the enrichment *in excess of* the natural ^{18}O content) in the carbonyl-oxygen position could be determined in both 1-phenylallyl and cinnamyl *p*-nitrobenzoate by infrared differential absorption measurements using the 6 μ carbonyl stretching

Acid concn. (M)	$\tau_{\frac{1}{2}}$ (min.)	10^5R_E	x	y	A_0	A_∞	$\bar{x}$	$\bar{A}$	t'
0·00025	77	0·23	11·5	70·8	7150	12·5	7·9	1692	465
0·00025	86	0·20	10·7	104	8650	15·0	6·4	2557	405
0·00056	160	0·24	—	—	—	—	—	—	—
0·0013	200	0·45	—	—	—	—	—	—	—
0·0020	325	0·42	—	—	—	—	—	—	—
0·0045	310	0·98	12·0	58·0	810	20·8	7·6	424·8	580
0·0096	300	2·10	19·7	36·5	409	21·8	13·4	142·8	1320
0·015	300	3·20	13·5	63·0	275	22·2	7·8	180	440
0·018	330	3·43	—	—	—	—	—	—	—
0·027	325	4·98	13·0	30·8	231	31·4	5·14	163·4	420
0·037	315	6·70	5·60	15·7	77·2	13·8	3·04	56·3	390
0·045	280	8·80	6·50	36·6	117	24·5	3·4	88	325
0·067	240	13·9	7·90	21·2	82·5	23·2	4·2	63·1	305
0·090	264	15·3	6·95	14·4	51·8	17·9	3·8	40·6	330

band. Since the cinnamyl ester was the more readily purified after separation from reaction mixtures, the interchange of oxygen functions was followed by observations upon the carbonyl-^{18}O enrichment of this ester. The values found for various stages of rearrangement are plotted *versus* time in Fig. 2. The theoretical curve was derived on the assumption that " scrambling " of the oxygen atoms by way of carboxyl group exchange with traces of *p*-nitrobenzoic acid takes place at a rate suggested by the ^{14}C studies as follows:

The reactants were considered to have carboxyl isotopic contents shown:

α-Ester: a { $-O-C(=^{18}O)$ y ; $-^{18}O-C(=O)$ x ; $-O-C(=O)$ }

Acid: b { $O-C(=^{18}O)$ $zb/2a$; $-^{18}O-C(=O)$ $zb/2a$; $-O-C(=O)$ }

where a, b, x, y, z $(= x + y)$ are concentrations (mole $l.^{-1}$), R_e = rate of exchange (mole $l.^{-1}$ $min.^{-1}$) $= k_e a$, and k_r = 1st-order rate constant of rearrangement.

Case I: As a result of exchange without rearrangement (k_s):

$$dx/dt = R_e(a - x)z/2a^2 - R_e x(1 - z/2a)/a - k_r x$$

Since $z = z_0 \exp(-k_r t)$

$$dx/dt + (k_e + k_r)x = k_e z_0 \exp(-k_r t)$$

which can be integrated to

$$x = \tfrac{1}{2}z_0 \exp(-k_r t) + C \exp[-(k_e + k_r)t]$$

If $x = 0$ when $t = 0$, C (the constant of integration) $= -\tfrac{1}{2}z_0$, then

$$x = \tfrac{1}{2}z_0\{\exp(-k_r t) - \exp[-(k_e + k_r)t]\}$$

The concentration of carbonyl-labelled γ-ester produced by intramolecular rearrangement between t and $(t + dt)$ would be $k_r x_t\, dt$.

Hence the concentration of such ester produced from time 0 to t' would be $\int_0^{t'} k_r x\, dt$. The enrichment of the γ-ester with reference to the carbonyl position would thus be $\int_0^{t'} (k_r x\, dt)/a_0[1 - \exp(-k_r t)]$, since $a_0[1 - \exp(k_r t)]$ would be the overall γ-ester concentration at t'; from above therefore

$$\text{Enrichment} = (z_0/2a_0)\{1 - k_r[1 - \exp(-k_e + k_r)t]/(k_e + k_r)[1 - \exp(-k_r t)]\} \quad . \quad (1)$$

XUM

Case II: As a result of exchange accompanied by rearrangement (R_2) (concn. of cinnamyl ester, $^-O-C=^{18}O = x'$):

$$dx'/dt = k_e z/2a \text{ (there being no reverse reaction)}$$

$$= \tfrac{1}{2}k_e z$$

and similarly

$$\text{Enrichment} = k_e z_0/2k_r a_0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Since the ^{14}C experiments indicated that both kinds of exchange were probable in the ratio k_e (Case I) : k_e (Case II) of $\sim 3 : 1$ at low acid concentration, the enrichment resulting would be the sum of (1) and (2), the k_e appropriate in each case being used. The curve shown (Fig. 2) results from the substitution in the above expressions of the following values: k_e for reaction R_3 $0{\cdot}30 \times 10^{-4}$ min.$^{-1}$; k_e for reaction R_2 $0{\cdot}13 \times 10^{-4}$ min.$^{-1}$; k_r $0{\cdot}89 \times 10^{-4}$ min.$^{-1}$; *i.e.*, k_e (Case I) + k_e (Case II) = $0{\cdot}43 \times 10^{-4}$ min.$^{-1}$, which corresponds to a total rate of exchange of $0{\cdot}75 \times 10^{-5}$ mole l.$^{-1}$ min.$^{-1}$. This would require an acid concentration of *ca.* 4×10^{-3}M, a value consistent with our earlier findings (preceding paper).

Discussion

If *p*-nitrobenzoic acid participated in the rearrangements in any way other than by simple proton-donation either with (as in the catalysis by halogen acids of the rearrangement of allylic alcohols) or without dissociation of the O–H bond, interchange of the carboxyl-^{14}C between the ester and the acid would be expected. In particular, if the rate-controlling step were ionisation of the ester to be followed by ion-recombination at either the α- or the γ-carbon atom, the rate of ^{14}C exchange could not depend in a simple linear manner on the concentration of the acid.

The rate (R) of isotopic exchange between two chemical species whose concentrations are [X] and [Y] respectively has been expressed by Duffield and Calvin [11] as:

$$R = 0{\cdot}693[X][Y]/\tau_{\frac{1}{2}}([X] + [Y])$$

If [X] and [Y] differ widely this leads in the case of a bimolecular exchange process ($R = k_2[X][Y]$) to nearly constant values of $\tau_{\frac{1}{2}}$ when as in this investigation the lesser of [X] and [Y] only is varied.

It is evident from the observed values of $\tau_{\frac{1}{2}}$ that for acid concentrations greater than about 0·002M (that is, the minimum value reached under "normal" experimental conditions), an exchange (of anionic group) occurred between the ester and *p*-nitrobenzoic acid present, which was bimolecular (of the first order with respect to acid concentration). Further, the appearance of radioactivity in cinnamyl *p*-nitrobenzoate in the early stage of reaction cannot have been the result of rearrangement (intramolecularly) of exchange-labelled 1-phenylallyl *p*-nitrobenzoate since the specific activity of the rearranged product by this route could never at any instant be higher than that of the starting material. The generally higher specific activity of the former than of the latter isolated at a time not much greater than the half time of exchange (*i.e.*, when the specific activity of the acid is still significantly higher than that of the 1-phenylallyl *p*-nitrobenzoate) indicates direct participation of the acid in the act of rearrangement.

This, however, cannot have been the only route to cinnamyl *p*-nitrobenzoate; the total rate of exchange was always less than the total rate of rearrangement, and a large fraction of the former resulted in no rearrangement (to give radioactive 1-phenylallyl *p*-nitrobenzoate). Thus we were led to consider:

$$R_e = R_2 + R_3$$

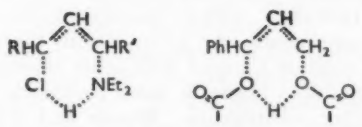
$$R_r = R_1 + R_2$$

where rearrangement without exchange $= R_1$, rearrangement with exchange $= R_2$,

[11] Duffield and Calvin, *J. Amer. Chem. Soc.*, 1946, **68**, 557.

exchange without rearrangement $= R_3$, and (possibly) exchange after rearrangement $= R_4$.

Except at the lowest concentration of acid, both R_2 and R_3 were found to be of the first order with respect to acid concentration. R_3 may be analogous to weakly alkaline hydrolysis in aqueous media which, contrary to the findings of Kenyon, Partridge, and Phillips,[12] takes place without rearrangement. Since it has been shown that anions are ineffective in promoting bimolecular rearrangement in this case (preceding paper), R_2 must involve both carboxylate anion and proton in a more or less concerted attack. The linear relation of rate to concentration suggests that undissociated *p*-nitrobenzoic acid acts as a kinetic unit. This interpretation is open to objection on the grounds of the known tendency of carboxylic acids to form dimers in this type of solvent. If this were so bimolecular reaction with the *p*-nitrobenzoic acid molecule would be linearly related to some fractional power of the total acid concentration. Dimer formation in carboxylic acids is known, however, to be reduced by increase of temperature, dielectric constant of the medium, and acid dissociation constant, and measurement of the elevation of the b. p. of chlorobenzene by *p*-nitrobenzoic acid showed no increase in the effective molecular weight of the latter greater than experimental error. We conclude therefore that bimolecular rearrangement is initiated by the combined attack of proton and anion. The manner in which a proton is shared between the anion and the attacked allylic system remains obscure since nothing is known of the dissociation of *p*-nitrobenzoic acid in this medium. It may, however, be conjectured that a more or less synchronous bond rearrangement results from the arrangement of the reagents to form a six-atom hydrogen-bridged ring analogous to that postulated for the rearrangement accompanying attack by primary and secondary amines:[5,6]



The acid-catalysis of rearrangement without exchange (R_1) is also undoubtedly to be attributed to an initial proton-attachment at the alkoxyl-oxygen atom, resulting in a weakening of the alkyl–oxygen link and partial redistribution of the electrons of the allylic double bond, as discussed for the proton-catalysed rearrangement of allylic alcohols.[8] This cannot, however, account for the whole of the rearrangement, as implied by the comment of De Wolfe and Young[13] on the preliminary communication of these results. It is, of course, most unlikely that in the solvent used, a " free " proton is at any stage obtained; its transfer from a molecule of *p*-nitrobenzoic acid to an ester molecule must result from an intimate colligation of the two—catalysis is bimolecular as the kinetic data show.

As the concentration of acid was progressively reduced, however, rearrangement tended to become entirely intramolecular in the sense that migration of the carboxyl group was not diverted by the few acid molecules present. We would not maintain that this evidence alone demonstrates this reaction to proceed without any charge development whatsoever; we hold, however, that to describe the fragments as ionic is to distort the original meaning of the term.

The investigation of this reaction by means of ^{18}O demonstrated clearly that the migrating group was not free in the ionic sense. The small amount of " scrambling " which took place in this case would be entirely explained in terms of exchange of carboxyl group with the inevitable trace of *p*-nitrobenzoic acid rapidly produced.

Imperial College of Science and Technology,
London, S.W.7.

[*Received, January 9th*, 1958.]

[12] Kenyon, Partridge, and Phillips, *J.*, 1937, 207.
[13] De Wolfe and Young, *Chem. Rev.*, 1956, **56**, 776.

481. *Infrared Spectra of Boron Compounds.*

By L. J. Bellamy, W. Gerrard, M. F. Lappert, and R. L. Williams.

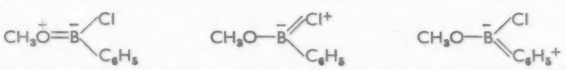
Many spectra of organoboron compounds and of some boron hydrides have been obtained. The positions of a number of characteristic group frequencies were determined and are discussed.

Infrared spectra of organoboron compounds and boron hydrides have received little systematic study, but a few specific correlations are available, notably the assignment of a B–O stretching mode to the 1340 cm.$^{-1}$ region by Werner and O'Brien.[1,2] This has been supported by Dandegaonker, Gerrard, and Lappert [3] who also discussed the possible assignment of the B–Cl stretching frequency near 900 cm.$^{-1}$. The spectra of some derivatives of diphenylboronous acid have also been discussed,[4] and there have been several detailed studies of individual molecules of both organoboron compounds and boron hydrides.

During chemical studies in this field many infrared spectra have been accumulated. We have reviewed these to see how far existing correlations could be confirmed and if new ones might be added, and now give our results.

Organoboron Compounds.—The B–O *stretching frequency.* This was identified as falling at 1340 ± 10 cm.$^{-1}$ in boronite esters [1] and mixed esters [2] (although the band in *cyclo*hexyl diphenyl borate was displaced to 1363 cm.$^{-1}$). Dandegaonker *et al.*[3] found the absorption between 1350 and 1330 cm.$^{-1}$ in phenylchloroboronites and in phenylboronates, and in diphenylboronous acid and its derivatives it occurs [4] at 1325 ± 2 cm.$^{-1}$.

We have examined 56 borates, boronates, and boronites. In all, a strong absorption is found in the range 1350—1310 cm.$^{-1}$, with 51 absorbing within the narrower limits 1346—1316 cm.$^{-1}$. The band is very intense and is thus readily identified. Its high frequency, intensity, and stability of position contrast with other absorptions of this type, such as that of the P–O link, which fall at markedly lower frequencies and tend to be influenced more by the nature of other substituents. Werner and O'Brien [1] suggested that the B–O bond has some double-bond character, and the stability in position of this absorption and its high intensity are probably associated with this. In all the compounds studied the boron valencies are linked with phenyl, chlorine, or oxygen atoms each of which can donate electrons to make up the boron octet. Resonance can therefore be expected between canonical forms, which in a compound such as methyl phenylchloroboronite can be represented as:



The occurrence of resonance of this type is independently supported by dipole-moment studies.[5] This would be expected to lead to higher frequencies and intensities in the B–O link, as is confirmed by the strong band near 1340 cm.$^{-1}$ being absent from the spectra of these compounds when they are coupled with strong electron donors such as pyridine or other tertiary bases. In such couples resonance of this type is largely suppressed and it becomes difficult to recognise the less intense B–O absorption which occurs at lower frequencies. 2-Aminoethyl diphenylboronite behaves similarly and does not absorb near 1340 cm.$^{-1}$, presumably owing to the lengthening of the B–O bond due to internal complex formation.[6] This correlation is therefore only applicable to situations in which the boron octet is not fully completed.

[1] Werner and O'Brien, *Austral. J. Chem.*, 1955, **8**, 355.
[2] *Idem, ibid.*, 1956, **9**, 137.
[3] Dandegaonker, Gerrard, and Lappert, *J.*, 1957, 2872.
[4] Abel, Gerrard, and Lappert, *ibid.*, p. 3833.
[5] Curran, McCusker, and Makowski, *J. Amer. Chem. Soc.*, 1957, **79**, 5188.
[6] Letsinger and Skoog, *ibid.*, 1955, **77**, 2491.

XUM

B–Cl. The asymmetric and symmetric B–Cl stretching frequencies of boron trichloride have been assigned [7] at 955 cm.$^{-1}$ (E) and 471 cm.$^{-1}$ (A_1), and Dandegaonker *et al.*[3] noted a strong band near 900 cm.$^{-1}$ in alkyl phenylchloroboronites which they assign to the B–Cl mode. We have confirmed this observation in thirteen compounds of this type in all of which a strong band occurs between 909 and 893 cm.$^{-1}$. Diphenylboron chloride absorbs strongly at 895 cm.$^{-1}$ and phenylboron dichloride at 885 cm.$^{-1}$, but in di-*n*-butyl chloroboronate the frequency falls to 858 cm.$^{-1}$, which may be due to the increased electron-donating powers of the oxygen atoms. In bis(diethylamino)boron chloride this process is carried a stage further and it is no longer possible to identify a B–Cl absorption from amongst a number of less intense bands at lower frequencies. Similarly the 895 cm.$^{-1}$ band of diphenylboron chloride is removed by complex formation with tertiary bases.

B–*Aryl*. Both the P–Aryl [9] and Si–Aryl [10] linkages have been assigned a characteristic frequency near 1430 cm.$^{-1}$, and the former absorbs also near 1000 and the latter near 1100 cm.$^{-1}$. In the 42 B–Aryl compounds studied we also find a strong sharp absorption between 1440 and 1430 cm.$^{-1}$. This appears to be the 1470—1438 cm.$^{-1}$ band of monosubstituted aromatic compounds,[11] and the fact that the lowest of these values relates to iodobenzene in which the electronegativity of the substituent is also low, may be significant. The origin of the second band is less clear and its position varies.

In a series of sixteen compounds containing the residue Ph_2B a strong absorption is found between 1280 and 1250 cm.$^{-1}$ which can reasonably be assigned to the Ph–B group, particularly as it is strongly marked in diphenylboron chloride and in the corresponding bromide. In alkyl phenylchloroboronites the band shifts towards lower frequencies and is now found (11 compounds) as a strong absorption between 1220 and 1198 cm.$^{-1}$. In dialkyl phenylboronates no strong bands are found in either of these regions but a new strong one in the range 1175—1125 cm.$^{-1}$ (13 compounds).

One other interesting feature of these spectra is the splitting of the out-of-plane CH aromatic deformation absorptions which occurs when more than one aromatic ring is directly attached to the boron atom. This has previously been reported by Abel *et al.*[4] who reported a separation of 20 cm.$^{-1}$ in the " doublet " produced. This finding has been confirmed in all cases studied here and applies also to the spectrum of sodium tetraphenylboron.

B–CH_3 *and* B–N *frequencies*. The asymmetric and symmetric deformations of a methyl group attached to an element X are usually constant in position and depend in part upon the electronegativity of X.[12,13] The symmetric one is particularly characteristic and useful correlations arise from this fact. For boron, considerations of electronegativity [12] suggest that the symmetric frequency should fall in the 1350—1300 cm.$^{-1}$ range. Trimethylboron [14] absorbs at 1460 cm.$^{-1}$ and 1305 cm.$^{-1}$ and these bands can reasonably be assigned to the asymmetric and symmetric methyl deformation modes. In addition, nine compounds containing the CH_3–B group were studied by Becher *et al.*[8,14,15] in either the Raman or the infrared region. All show comparable bands which fall in the ranges 1460—1405 cm.$^{-1}$ and 1320—1280 cm.$^{-1}$ and can be similarly assigned. Although less specific than most other CH_3–X frequencies these may well be useful in particular cases.

The compounds studied by Becher *et al.*[15] include instances in which the boron is directly attached to nitrogen. In $Me_2B{\cdot}NH{\cdot}C_6H_5$, for example, the B–N absorption is

[7] Lindeman and Wilson, *J. Chem. Phys.*, 1956, **24**, 242.
[8] Becher, *Z. anorg. Chem.*, 1953, **271**, 243.
[9] Daasch and Smith, *Analyt. Chem.*, 1951, **23**, 853.
[10] Young, Servais, Currie, and Hunter, *J. Amer. Chem. Soc.*, 1948, **70**, 3758.
[11] Josien and Lebas, *Bull. Soc. chim. France*, 1956, **53**, 57.
[12] Sheppard, *Trans. Faraday Soc.*, 1955, **51**, 1465.
[13] Bellamy and Williams, *J.*, 1956, 2753.
[14] Goubeau and Becher, *Z. anorg. Chem.*, 1952, **268**, 1.
[15] Becher, *ibid.*, 1957, **289**, 262; Becher and Goubeau, *ibid.*, 1952, **268**, 133.

assigned at 1332 cm.$^{-1}$, and 1343 cm.$^{-1}$ is quoted for the corresponding pyrrole derivative. The B–N link is likely to possess double-bond character in the same way as the B–O link, and the assignment is therefore reasonable, particularly as four other compounds they studied appear to show strong bands in the 1378—1332 cm.$^{-1}$ region, and the complex of trimethylboron with ammonia (in which the B–N link has no double-bond character) shows no comparable band [8] and the B–N stretching frequency is then assigned at 1105 cm.$^{-1}$. We have observed bands near 1350 cm.$^{-1}$ for $(Bu^n_2N)_3B$ and $(Et_2N)_3B$, but not for complexes of boron trichloride with secondary bases. Whilst this correlation must be regarded as tentative it should be realised that both the B–O and B–N stretching absorptions are liable to occur at similar frequencies.

Boron Hydrides.—The spectra of many boron hydrides are available in the literature. Diborane has been studied,[16,18] and detailed assignments have been given for pentaborane,[19] dimethylaminodiborane,[20] and dimethylaminoborine.[21] The spectra of tetraborane, pentaborane, and dihydropentaborane have also been described,[22] but no detailed assignments were given. We re-examined some of these materials and added the spectra of decaborane and its monoethyl, diethyl, and monoiodo-derivatives. Four different types of boron–hydrogen link have been described in the various hydrides and these differences should be reflected in the infrared spectra. In addition to the well-known bridged-ring hydrogen atoms, normal BH_2 and BH groups occur in most cases. The latter are, however, divisible into two classes as nuclear resonance studies have shown [23] that the B–H links at apical positions in compounds such as pentaborane are characteristically different from those at other positions.

B–H *Stretching frequencies.* The hydrogen atoms which form bridge rings between two boron atoms perform breathing motions which cause a series of absorptions in the range 2220—1600 cm.$^{-1}$. These have been defined in diborane and pentaborane and similar bands are found in all the other compounds studied which contain this structure. Their number and position vary considerably, however, and although there is usually at least one band in the 1900—1800 cm.$^{-1}$ range there is no other regularity. The normal BH and BH_2 stretching modes always fall in the range 2630—2350 cm.$^{-1}$. There appears to be no basic frequency difference but the BH_2 group can be identified by the doubling due to asymmetric and symmetric modes. Similarly no difference could be detected at the resolution available between the stretching frequencies of the normal and apical BH groups in compounds such as decaborane and pentaborane.

B–H *Deformation frequencies.* The BH_2 " scissoring " mode in diborane absorbs at 1180 cm.$^{-1}$ and a corresponding band, which is sometimes a closely separated doublet, can be identified in the range 1205—1140 cm.$^{-1}$ in all compounds containing this group. The 973 cm.$^{-1}$ BH_2 wagging mode of diborane can similarly be identified in other materials in the range 975—945 cm.$^{-1}$. Neither of these bands appears in compounds such as decaborane which contain only BH links. The identification of the deformation frequencies of the latter must necessarily be more tentative. A band occurs very near 900 cm.$^{-1}$ for decaborane, pentaborane, tetraborane, and dihydropentaborane (all of which contain apical BH links) which is not present for the few compounds studied which lack this structure. Further, the band is much weaker for monoethyldecaborane. This suggests a possible correlation which should be studied further. The deformation frequency of normal BH links appears to occur elsewhere but is less easy to identify. Hrostowski and Pimentel [19] assign absorptions in the 1620—1440 cm.$^{-1}$ region to this

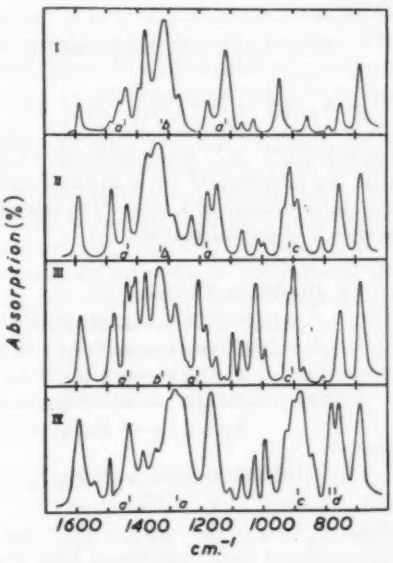
[16] Price, *J. Chem. Phys.*, 1948, **16**, 894.
[17] Lord and Nielsen, *ibid.*, 1951, **19**, 1.
[18] Anderson and Barker, *ibid.*, 1950, **18**, 698.
[19] Hrostowski and Pimentel, *J. Amer. Chem. Soc.*, 1954, **76**, 998.
[20] Mann, *J. Chem. Phys.*, 1954, **22**, 70.
[21] Price, Fraser, Robinson, and Longuet-Higgins, *Discuss. Faraday Soc.*, 1950, **9**, 131.
[22] McCarty, Smith, and McDonald, *Analyt. Chem.*, 1954, **26**, 1027.
[23] Schaeffer, Shoolery, and Jones, *J. Amer. Chem. Soc.*, 1957, **79**, 4606.

XUM

vibration in pentaborane and bands in this region are found in the other appropriate compounds. The frequency appears abnormally high however in relation to those discussed above, and as all these materials also contain bridged-ring structures it is possible that these absorptions arise from these. An alternative, and in some ways more attractive, assignment would be the region 1075—1010 cm.$^{-1}$ in which a common band is again found in the series of compounds containing B–H links at non-apical positions. The present data are however insufficient to enable these possibilities to be differentiated.

Experimental.—Spectra were measured either in a G.S.2 Grubb-Parsons double-beam grating spectrometer fitted with a 2400 line/inch N.P.L. replica grating, or in a Grubb-Parsons S.3A double-beam model with a sodium chloride prism. Samples were studied as liquid films, as solid mulls in paraffin oil, or as vapours as appropriate.

Results.—As the spectra have been submitted for reproduction in the D.M.S. punched-card system, only relevant portions are discussed. However, to present an overall picture of the results, four typical spectra (I, di-*n*-propyl phenylboronate; II phenyl phenylchloroboronite; III, ethyl phenylchloroboronite; IV, diphenylboron chloride) are shown in the Figure. Specific assignments are indicated: *a*, B–Ph; *b*, B–O; *c*, B–Cl; *d*, splitting of C–H band in the phenyl rings.



We thank Mr. H. Pyszora for experimental assistance.

MINISTRY OF SUPPLY, EXPLOSIVES RESEARCH AND DEVELOPMENT ESTABLISHMENT, WALTHAM ABBEY, ESSEX.
THE NORTHERN POLYTECHNIC, LONDON, N.7. [*Received, January 27th*, 1958.]

NOTES.

482. *Nitrous Acid Equilibria in Perchloric Acid.*

By T. A. TURNEY and G. A. WRIGHT.

THE following equilibria are of interest in considering the reactivity of nitrous acid in acidic media:

$$HONO + H_3O^+ \rightleftharpoons NO^+ + 2H_2O \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$2HONO \rightleftharpoons N_2O_3 + H_2O \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Recently,[1] the proportion of nitrosonium ion present in solutions of sodium nitrite in concentrated perchloric acid was measured spectrophotometrically, but no equilibrium constant was found. We have now estimated the equilibrium constants of the two reactions by considering thermodynamic cycles, and determined the equilibrium constant for reaction (1) spectrophotometrically.

Thermodynamic Calculations.—Two cycles of hypothetical reactions were used involving

[1] Singer and Vamplew, *J.*, 1956, 3971.

the gas phase in which the ionisation potential of nitric oxide and the free energy of formation of dinitrogen trioxide are known.

(1) *Nitrosonium ion.*

$$\begin{aligned} HONO(aq.) + H^+(aq.) &\longrightarrow NO(g.) + H_2O(l.) & \Delta G_a^\circ &= -133{\cdot}1 \text{ kcal. mole}^{-1} \\ NO(g.) &\longrightarrow NO^+(g.) & \Delta G_b^\circ &= 219{\cdot}0 \text{ kcal. mole}^{-1} \\ NO^+(g.) &\longrightarrow NO^+(aq.) & \Delta G_c^\circ &= -80{\cdot}2 \text{ kcal. mole}^{-1} \end{aligned}$$

Hence,

$$HONO(aq.) + H^+(aq.) \longrightarrow NO^+(aq.) + H_2O(l.) \quad \Delta G^\circ{}_1 = 5{\cdot}7 \text{ kcal. mole}^{-1}$$

Thus $K_1 = 7 \times 10^{-5}$ (25°). ΔG_a° was obtained from the standard free energies of formation of the substances involved.[2] ΔG_b° was calculated from the ionisation energy of nitric oxide.[3] ΔG_c° was interpolated from the data for the alkali-metal ions,[4] by assuming that the nitrosonium ion is approximately a sphere of radius 1·11 Å[3] and correcting to a standard pressure of 1 atm. The uncertainty in this interpolation is the limitation on the accuracy of the calculation.

(2) *Dinitrogen trioxide.*

$$\begin{aligned} 2HONO(aq.) &\longrightarrow 2HONO(g.) & \Delta G_a^\circ &= 4{\cdot}16 \text{ kcal. mole}^{-1} \\ 2HONO(g.) &\longrightarrow NO(g.) + NO_2(g.) + H_2O(g.) & \Delta G_b^\circ &= 0{\cdot}30 \text{ kcal. mole}^{-1} \\ H_2O(g.) &\longrightarrow H_2O(l.) & \Delta G_c^\circ &= -2{\cdot}06 \text{ kcal. mole}^{-1} \\ NO(g.) + NO_2(g.) &\longrightarrow N_2O_3(g.) & \Delta G_d^\circ &= 0{\cdot}38 \text{ kcal. mole}^{-1} \\ N_2O_3(g.) &\longrightarrow N_2O_3(aq.) & \Delta G_e^\circ &= 0 \end{aligned}$$

Hence

$$2HONO(aq.) \longrightarrow N_2O_3(aq.) + H_2O(l.) \quad \Delta G_2^\circ = 2{\cdot}78 \text{ kcal. mole}^{-1}$$

Thus $K_2 = 9 \times 10^{-3}$ (25°). ΔG_a° and ΔG_b° were obtained from Wayne and Yost's calculations.[5] ΔG_c° was found from the standard free energies of formation.[2] ΔG_d° has been measured experimentally.[6] ΔG_e° cannot be found exactly but was estimated approximately by plotting the hydration energies of similar molecules against their parachors (a convenient measure of molecular volume) and extrapolating to find the value for dinitrogen trioxide.

Experimental.—Solutions of nitrous acid were made by dissolving " AnalaR " sodium nitrite in aqueous " AnalaR " perchloric acid. Absorption was measured on a Beckman model D.U. spectrophotometer with a hydrogen lamp and photomultiplier attachment. The total concentration of all the nitrous acid species present was determined colorimetrically [7] through the diazotisation of sulphanilic acid and coupling with α-naphthylamine. Dilute solutions of nitrous acid in 50% perchloric acid solution decompose steadily. The extent of this decomposition was measured by recording the change of optical density with time. Also, the additional decomposition due to disturbance of the solution during transfer by pipette was estimated similarly. The sum of these errors in the 3 min. required to complete the absorbance readings and commence the analysis was not greater than 4%. The procedure used was rapidly to measure the optical densities of the solution at four selected wavelengths, then immediately transfer 1 ml. of the solution to a flask containing 1 ml. of the sulphanilic acid reagent. This strongly acidic mixture diazotises rapidly, so minimising errors due to decomposition.

[2] Latimer, " Oxidation Potentials," Prentice-Hall, New York, 1952.
[3] Addison and Lewis, *Quart. Rev.*, 1955, **9**, 115.
[4] Robinson and Stokes, " Electrolyte Solutions," Butterworths, London, 1955.
[5] Wayne and Yost, *J. Chem. Phys.*, 1951, **19**, 41.
[6] Beattie and Bell, *J.*, 1957, 1686.
[7] Rider and Mellon, *Ind. Eng. Chem. Anal.*, 1946, **18**, 96.

XUM

Results and Discussion.—In 10% perchloric acid the known spectrum of the nitrous acid molecule was observed.[8, 9, 10] Four main absorption peaks occurred at 347 mμ (ε_1 39), 358 mμ (ε_1 54), 372 mμ (ε_1 55), and 386 mμ (ε_1 33). The spectrum persisted unchanged in up to 40% perchloric acid. Above 55% perchloric acid a single intense, broad band with a maximum at 260 mμ (ε *ca.* 4000) appeared and was taken to be the spectrum of the nitrosonium ion. This spectrum remained constant in shape but the extinction coefficients varied considerably as the perchloric acid concentration or the nitrous acid concentration changed. This may be due to some hydration effect of the nitrosonium ion. In the region 45—55% perchloric acid the spectra corresponded to a mixture of molecular nitrous acid and nitrosonium ions. There was no sign of dinitrogen trioxide in these dilute solutions of nitrous acid (10^{-3} mole $l.^{-1}$); this is as expected from the calculated equilibrium constants. These results generally agree with those of previous workers,[1] but there are some differences of detail.

To determine K_1 from the absorption spectra the ratio $R = [NO^+]/[HNO_2]$ in the region of the mixed spectra must be determined, so the four main absorption peaks of molecular nitrous acid were measured, these being reliably known. The spectrum of the nitrosonium ion is unsuitable because it does not obey Beer's law. However, the shape of the absorption curve of nitrosonium ion is fixed and the extinction coefficients in any solution are given by $x\varepsilon_2$, where x is a factor for that solution and ε_2 is the value for 60% perchloric acid, *e.g.*, at 347 mμ (ε_2 131), 358 mμ (ε_2 53), 372 mμ (ε_2 18), and 386 mμ (ε_2 6). At any wavelength, $D = \varepsilon_1[HNO_2] + x\varepsilon_2[NO^+]$. Also, since $C = [HNO_2] + [NO^+]$, then $D/C = (\varepsilon_1 + x\varepsilon_2 R)/(1 + R)$. If the optical density D is measured at the four selected wavelengths, then there are four such equations which can be solved in pairs to eliminate x and give R. The mean values of R so determined are given for six solutions in Table 1.

TABLE 1. *Typical determinations of R at* $[HClO_4] = 10{\cdot}40$m.

	D/C				
10^4C (M)	347 mμ	358 mμ	372 mμ	386 mμ	R
25·0	60·4	48·8	36·8	22·0	0·65
29·2	60·6	47·3	35·6	21·6	0·69
33·2	62·0	49·1	37·1	22·6	0·62
40·9	65·3	50·6	37·9	23·5	0·58
41·1	64·5	50·1	36·7	23·1	0·62
44·8	69·6	55·6	40·9	24·6	0·49

TABLE 2. *Determination of pK_1 for various molalities, m, of perchloric acid.*

m	H_0	J_0''	R	pK_1
10·20	−3·74	−4·73	0·26	7·05
10·40	−3·79	−4·82	0·61	6·77
10·50	−3·81	−4·86	0·97	6·61
10·71	−3·90	−5·03	1·01	6·77
10·86	−3·94	−5·10	1·46	6·68
10·99	−4·00	−5·22	1·81	6·70

The values of R (mean 0·61 ± 0·05) show some scatter and for this reason six determinations were carried out at each concentration of perchloric acid used. By this method R could be measured conveniently over only a small range of perchloric acid concentrations (50—53%). There is no systematic variation of R with nitrous acid concentration.

The most satisfactory method of finding K_1 is to use the acidity function[11] $J_0 = -pK_1 - \log R$. J_0 is not known for perchloric acid but a reasonable approximation to it has been suggested:[12]

$$J_0'' = 2H_0 + \log [H_3O^+]_N + 1{\cdot}74$$

H_0 is known for perchloric acid,[11] and hence pK_1 can be found as shown in Table 2. The subscript N indicates (see ref. 12) that H_3O^+ is measured in mole-fraction units.

Values of pK_1 (mean 6·76) are reasonably constant, giving $K_1 = 2 \times 10^{-7}$ (20°). Singer and Vamplew's results [1] can be treated in a similar fashion, yielding $K_1 = 3 \times 10^{-7}$. The disagreement with the predicted constant is due partly to the uncertainty of the free

[8] Kortum, *Z. phys. Chem.*, 1939, **43**, *B*, 418.
[9] Bayliss and Watts, *Austral. J. Chem.*, 1956, **9**, 319.
[10] Longstaff and Singer, *J.*, 1954, 2604.
[11] Paul and Long, *Chem. Rev.*, 1957, **57**, 1.
[12] Gold, *J.*, 1955, 1263.

XUM

energy of hydration of the nitrosonium ion and partly to the fact that the approximate J_0'' values have uncertain absolute magnitudes although their variation with acid concentration is satisfactory.

One of us (T. A. T.) thanks the New Zealand University Research Grants Committee for a grant.

UNIVERSITY OF AUCKLAND, NEW ZEALAND. [*Received, October 2nd,* 1957.]

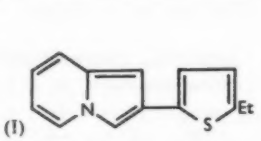
---

483. *Thiophen Derivatives. Part XII.* Some Derivatives of 2-Ethylthiophen.*

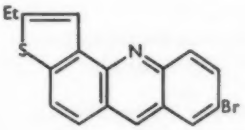
By NG. PH. BUU-HOÏ.

2-ETHYLTHIOPHEN was a convenient intermediate for the synthesis of thiophen compounds required for evaluation of the potential carcinogenic or choleretic activity. The present Note records the preparation of these new compounds, mostly ketones and nitrogen heterocyclic derivatives therefrom, none of which proved of biological interest.

2-Acetyl-5-ethylthiophen gave 2-(5-ethyl-2-thienyl)indole, and condensation of 2-bromoacetyl-5-ethylthiophen with α-picoline, followed by a Tschitschibabin cyclisation [1] of the quaternary picolinium salt, furnished 2-(5-ethyl-2-thienyl)pyrrocoline (I). Pfitzinger reaction of 5-bromoisatin with 2-acetyl-5-ethyl- and 2-ethyl-5-propionyl-thiophen afforded the 6-bromocinchoninic acids, which gave 6-bromoquinolines on thermal decarboxylation; α-naphthisatin [2] reacted with 2-acetyl-5-ethyl- but not with 2-ethyl-5-propionyl-thiophen under the same conditions.



(I)



(II)

Pfitzinger reaction of 5-bromoisatin with 2-ethyl-4 : 5 : 6 : 7-tetrahydro-4-oxothionaphthen [3] yielded 3-bromo-6 : 7-dihydro-5′-ethylthieno(2′ : 3′-8 : 9)acridine-5-carboxylic acid which, when heated above its m. p., underwent both decarboxylation and dehydrogenation, to give compound (II). Friedel–Crafts condensation of 2-ethylthiophen with phthalic anhydride afforded *o*-(5-ethyl-2-thenoyl)benzoic acid; similar Friedel–Crafts reactions with various aliphatic, aromatic, and thiophen acid chlorides yielded ketones listed in the Table.

Experimental.—*2-(5-Ethyl-2-thienyl)indole.* 2-Acetyl-5-ethylthiophen [4] (3 g.) was heated with phenylhydrazine (3 g.) at 120° until steam ceased to be evolved; to the crude phenylhydrazone, powdered fused zinc chloride (7 g.) was added, and the mixture heated above 200°, upon which a vigorous reaction set in. After cooling, aqueous acetic acid was added, the *indole* taken up in benzene, washed with water, and dried (Na_2SO_4), the solvent distilled off, and the residue fractionated *in vacuo*. The distillate (b. p. 240—250°/18 mm.) crystallised as prisms (2·5 g.), m. p. 130°, from light petroleum (Found: C, 73·7; H, 6·0. $C_{14}H_{13}NS$ requires C, 74·0; H, 5·8%). A similar reaction with 2-ethyl-5-propionylthiophen [5] gave 2-(5-ethyl-2-thienyl)-3-methylindole, a yellow oil, which gave a *picrate*, brown-violet needles, m. p. 126°, from light petroleum (Found: N, 11·6. $C_{21}H_{18}O_7N_4S$ requires N, 11·9%).

* Part XI, Buu-Hoï and Lavit, *J.*, 1958, 1721.

[1] Cf. Borrows and Holland, *Chem. Rev.*, 1948, **42**, 612; Buu-Hoï and Hoán, *Rec. Trav. chim.*, 1949, **68**, 454.

[2] Cf. Buu-Hoï and Cagniant, *Bull. Soc. chim. France*, 1946, **13**, 134.

[3] Buu-Hoï, Hoán, and Khôi, *J. Org. Chem.*, 1950, **15**, 957.

[4] Schleicher, *Ber.*, 1886, **19**, 660; Steinkopf, Frömmel, and Leo, *Annalen*, 1941, **546**, 199.

[5] Steinkopf, *Annalen*, 1923, **430**, 78.

2-(5-*Ethyl*-2-*thienyl*)*pyrrocoline* (I). 2-Acetyl-5-ethylthiophen (13 g.) with bromine (12·7 g.) in chloroform gave a bromo-ketone which decomposed on distillation *in vacuo*. A mixture of this compound (8 g.) and 2-picoline (4 g.) was heated in ethanol (10 c.c.) at 70° for a few minutes, and the picolinium salt obtained was precipitated by ether. An aqueous solution of this salt was brought to the boil with sodium hydrogen carbonate and the cyclisation *product* formed was collected and recrystallised from light petroleum, giving colourless prisms (5 g.), m. p. 119° (Found: N, 6·2. $C_{14}H_{13}NS$ requires N, 6·2%).

6-*Bromo*-2-(5-*ethyl*-2-*thienyl*)*cinchoninic acid*. 2-Acetyl-5-ethylthiophen [6] (3 g.) and 5-bromoisatin (4·4 g.) were heated with potassium hydroxide (3·5 g.) in ethanol (40 c.c.) for 5 hr.; after dilution with water and removal of the neutral impurities by ether the aqueous layer was acidified with acetic acid, and the precipitate recrystallised from ethanol as yellowish prisms (4 g.), m. p. 238° (Found: C, 52·8; H, 3·4. $C_{16}H_{12}O_2NSBr$ requires C, 53·0; H, 3·3%). 6-*Bromo*-2-(5-*ethyl*-2-*thienyl*)*quinoline*, prepared by heating this acid above its m. p., was purified *via* its picrate (deep yellow prisms, m. p. 188°, from ethanol), and formed yellowish leaflets, m. p. 107°, from ethanol (Found: C, 56·3; H, 3·9. $C_{15}H_{12}NSBr$ requires C, 56·6; H, 3·8%).

6-*Bromo*-2-(5-*ethyl*-2-*thienyl*)-3-*methylcinchoninic acid*. Prepared analogously (10 hours' refluxing), this *acid* (4·5 g.) formed pale yellow, sublimable needles, m. p. 239°, from ethanol (Found: C, 54·0; H, 3·5. $C_{17}H_{14}O_2NSBr$ requires C, 54·3; H, 3·7%). 6-*Bromo*-2-(5-*ethyl*-2-*thienyl*)-3-*methylquinoline* formed yellowish prisms, m. p. 80°, from ethanol (Found: C, 57·7; H, 4·5. $C_{16}H_{14}NSBr$ requires C, 57·8; H, 4·2%).

2-(5-*Ethyl*-2-*thienyl*)-7 : 8-*benzocinchoninic acid*. This *acid* (3 g.), similarly prepared, formed pale yellow, sublimable needles, m. p. 241°, from ethanol (Found: C, 71·8; H, 4·4. $C_{20}H_{15}O_2NS$ requires C, 72·1; H, 4·5%).

3-*Bromo*-6 : 7-*dihydro*-5′-*ethylthieno*(2′ : 3′-8 : 9)*acridine*-5-*carboxylic acid*, similarly prepared, formed yellowish prisms, m. p. 242°, from ethanol (Found: C, 55·5; H, 3·5. $C_{18}H_{14}O_2NSBr$ requires C, 55·7; H, 3·6%). Thermal decarboxylation of the acid (1·5 g.), and distillation of the product *in vacuo*, gave a resin which was converted into a *picrate*, forming orange-yellow prisms, m. p. 265° (decomp.), from ethanol (Found: N, 9·6. $C_{23}H_{15}O_7N_4SBr$ requires N, 9·8%). Basification of this picrate with ammonia yielded 3-*bromo*-5′-*ethylthieno*(2′ : 3′-8 : 9)*acridine* (II), crystallising as yellow prisms (0·2 g.), m. p. 150°, from ethanol (Found: C, 59·8; H, 3·4. $C_{17}H_{12}NSBr$ requires C, 59·6; H, 3·5%). That dehydrogenation had occurred was further shown by recovery of the base from treatment with chloranil in boiling xylene for 16 hr. This spontaneous dehydrogenation is in contrast with the relative stability of the analogous dihydrobenzacridines, which undergo dehydrogenation only when heated with chloranil.[7]

Ketones derived from 2-ethylthiophen.

Acyl deriv. of 2-ethylthiophen	B. p./mm.	M. p.	Formula	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H
*iso*Butyroyl	146—148°/20	—	$C_{10}H_{14}OS$	65·8	7·5	65·9	7·7
Octanoyl	196—198°/21	—	$C_{14}H_{22}OS$	70·3	9·2	70·6	9·3
p-Anisoyl [a]	241—243°/21	48°	$C_{14}H_{14}O_2S$	68·2	5·9	68·3	5·7
p-Hydroxybenzoyl [b]	—	126	$C_{13}H_{12}O_2S$	67·3	5·5	67·2	5·2
3-Allyl-4-hydroxybenzoyl [c]	—	84	$C_{16}H_{16}O_2S$	70·8	6·1	70·6	5·9
p-Toluoyl	—	69	$C_{14}H_{14}OS$	73·2	6·3	73·0	6·1
p-Ethylbenzoyl	—	56	$C_{15}H_{16}OS$	73·6	6·5	73·8	6·6
2-Thenoyl	—	41	$C_{11}H_8OS_2$	59·5	4·8	59·5	4·5
5-Chloro-2-thenoyl [d]	228—230°/23	—	$C_{11}H_7OS_2Cl$	51·8	3·3	51·5	3·5
5-Bromo-2-thenoyl	—	44	$C_{11}H_7OS_2Br$	44·1	3·2	43·9	3·0
5-Ethyl-2-thenoyl	—	81	$C_{12}H_{14}OS_2$	62·5	5·6	62·4	5·6
Fluorene-2-carbonyl [e]	—	89	$C_{20}H_{12}OS$	78·6	5·2	78·9	5·3
2-Furoyl	195—197°/20	—	$C_{11}H_8O_2S$	64·3	5·2	64·1	4·9

[a] All the solid ketones formed colourless prisms or leaflets from ligroin or benzene–ligroin. [b] Prepared by demethylation of the preceding ketone (10 g.) with boiling pyridine hydrochloride (30 g.), and recrystallised from benzene–ligroin. [c] Obtained by Claisen rearrangement of the allyl ether of the foregoing ketone (24 hours' boiling in dimethylaniline), and recrystallised from benzene–ligroin. [d] Solidified at room temperature. [e] Oxidised by sodium dichromate in acetic acid to a mixture of fluorenone-2-carboxylic acid and a compound which formed yellow prisms, m. p. 164°, from ethanol.

o-(5-*Ethyl*-2-*thenoyl*)*benzoic acid*. To a stirred mixture of 2-ethylthiophen (1·2 g.) and phthalic anhydride (1·5 g.) in carbon disulphide, aluminium chloride (1·5 g.) was added in small

[6] For other Pfitzinger reactions, see Cagniant and Cagniant, *Bull. Soc. chim. France*, 1952, 713.
[7] Buu-Hoï, Hoán, and Xuong, *J.*, 1952, 279.

XUM

portions at room temperature, and stirring was continued for 4 more hours. After decomposition with ice, the product was purified *via* its sodium salt; recrystallisation from *cyclo*hexane yielded fine, colourless prisms (0·5 g.), m. p. 103° (Found: C, 64·5; H, 4·8. $C_{14}H_{12}O_3S$ requires C, 64·6; H, 4·6%). With phenylhydrazine in boiling acetic acid, this *acid* gave a condensation product, m. p. 135°.

THE RADIUM INSTITUTE, UNIVERSITY OF PARIS. [*Received, December 30th*, 1957.]

---

484. *Oxygen Exchange between Nitric Acid and Water. Part IV.* The Nitration of 2-Mesitylethanesulphonic Acid.*

By C. A. BUNTON and G. STEDMAN.

IN Part II of this series [1] it was shown that the nitronium ion was an intermediate in both oxygen-exchange and aromatic nitration in aqueous nitric acid, and that the rate of the former was the rates of formation and hydration of the nitronium ion [2] (reactions 1 and 2):

$$2HNO_3 \underset{}{\overset{1}{\rightleftharpoons}} H_2NO_3^+ + NO_3^- \text{ (fast)}$$

$$H_2NO_3^+ \overset{2}{\rightleftharpoons} NO_2^+ + H_2O$$

$$\overset{3}{\downarrow} RH$$

$$RNO_2 + H^+$$

As the reactivities (or concentrations) of the aromatic compounds are increased they will capture an increasing proportion of the nitronium ions (reaction 3). Then the rate of nitration will approach that of oxygen exchange, and the kinetic order, which is first with respect to the aromatic compound when most of the nitronium ions are captured by water ($v_2 \gg v_3$), will decrease towards zero.

When the bulk reactivity of the aromatic compound is sufficiently greater than that of the water for sensibly all the nitronium ions to be captured by the aromatic compound ($v_3 \gg v_2$), the rate of nitration will be the rate of formation of nitronium ions and of oxygen-exchange, and independent of the nature or concentration of the aromatic compound. This is the well-known zero-order kinetic form for electrophilic aromatic substitution.[3]

In our earlier experiments [1] the aromatic compounds studied were not sufficiently reactive for the rate of nitration to equal that of oxygen exchange; the maximum nitration rates (observed for mesitylene-α- and *iso*durene-α²-sulphonic acid) were *ca.* 80% of those of oxygen exchange. 2-Mesitylethanesulphonic acid, in which the deactivating sulphonate group is further removed from the aromatic ring, was therefore synthesised, and its nitration followed dilatometrically.

The kinetic form, for most of the reaction (see Figure), was of zero order with respect to the aromatic compound. This region was followed by a very slow volume change, probably due to dinitration or demethylation, which did not interfere with determination of the nitration rate.

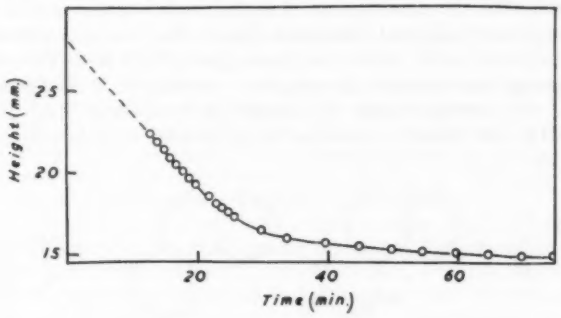
The zero-order rates are tabulated together with some data on *iso*durene-α²-sulphonic acid, and compared with the extrapolated rates of oxygen exchange. It was possible to obtain first-order nitration rates for all the compounds discussed in Part II,[1] but 2-mesitylethanesulphonic acid is too reactive for first-order nitrations to be studied.

* Part III, *J.*, 1953, 2653.

[1] Bunton and Halevi, *J.*, 1952, 4917.
[2] Bunton, Halevi, and Llewellyn, *J.*, 1952, 4913.
[3] Hughes, Ingold, and Reed, *J.*, 1950, 2400; de la Mare, Ketley, and Vernon, *J.*, 1954, 1290.

The zero-order nitration rates (k_o) for 2-mesitylethanesulphonic acid are *ca.* 15% greater than those of oxygen exchange (R). However the uncertainty in these extrapolated exchange rates [2] is of this order of magnitude, and the ionic-strength effect of the

Nitration at 0°. $[HNO_3]$ = 37·32 *mole* %. [ArH] = 0·244 *mole* %.



sodium 2-mesitylethanesulphonate will increase the rate of formation of the nitronium ion and hence of nitration.[1,4]

Experimental.—Preparation of materials. Mesitylene was chloromethylated, and the chloride converted into mesitylacetic acid *via* the cyanide.[5] The acid was reduced by lithium aluminium hydride and the 2-mesitylethyl alcohol brominated with phosphorus tribromide in dry benzene, to give *2-mesitylethyl bromide*, m. p. 74° (Found: C, 58·4; H, 6·6; Br, 35·0. $C_{11}H_{15}Br$ requires C, 58·2; H, 6·7; Br, 35·2%). The bromide was then converted into the sodium salt of the sulphonic acid by boiling aqueous sodium sulphite. It was characterised as its *S-benzylthiuronium salt*, m. p. 206° (Found: C, 58·1; H, 7·0; N, 7·4. $C_{19}H_{24}O_2N_2S_2$ requires C, 57·8; H, 6·6; N, 7·1%).

Kinetic measurements. The procedure was that described in Part II of this series.[1] The acid was used as its sodium salt.

Nitration of 2-mesitylethanesulphonic acid and iso*durene-α²-sulphonic acid at* 0°.

	2-Mesitylethanesulphonic acid					*iso*Durene-α²-sulphonic acid	
$[HNO_3]$ (mole %) ...	36·37	37·32	38·73	39·04	39·40	38·02	38·98
10^4k_o (mole % sec.$^{-1}$)	0·98	1·28	1·78	2·11	2·42	1·15	1·57
10^4R ,, ,,	0·81	1·10	1·74	1·92	2·15	1·44	1·82

The concentration of the aromatic compound was varied between 0·170 and 0·300 mole %.

WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES, UNIVERSITY COLLEGE, GOWER STREET, LONDON, W.C.1. [*Received, January 9th*, 1958.]

[4] Halberstadt, Hughes, and Ingold, *J.*, 1950, 2441.
[5] *Org. Synth.*, 1945, **25**, 65.

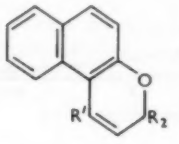
XUM

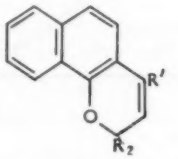
485. *Preparation of Some Naphthopyrans.*

By R. Livingstone, D. Miller, and R. B. Watson.

The action of anhydrous formic acid on a number of 6 : 6-disubstituted chromens was recently compared with the dimerisation of lapachenole [1] under similar conditions. The dimethylnaphthopyrans [2] (I*a*) and (II*a*) gave dimers when treated with anhydrous formic or methanolic sulphuric acid, unlike the analogues (II*b*) [2] and (I*b*) [3] which were inert. The 4-methyl group may hinder dimerisation sterically.[1] 6 : 6-Diethylnaphtho(2′ : 1′-2 : 3)pyran (I*c*), the corresponding 6 : 6-diphenyl compound (I*d*), and the 4-chloro-derivative [2] of (II*b*) also failed to dimerise when treated with formic acid or methanolic hydrogen chloride.

(I)	R	R′
a	Me	H
b	Me	Me
c	Et	H
d	Ph	H





(II)	R	R′
a	Me	H
b	Me	Me

6 : 6-Dimethylnaphtho(2′ : 1′-2 : 3)pyran (I*a*) with 2 : 4-dinitrophenylhydrazine in butanolic sulphuric acid [2] gave 2 : 2-dimethyl-5 : 6-benzochroman-4-one 2 : 4-dinitrophenylhydrazone. The authentic benzochromanone was prepared by the Fries rearrangement [4] of the ββ-dimethylacryloyl ester.[5] The other analogues (I*b*), (I*c*), (I*d*), and (II*b*), unlike (II*a*),[2] failed to react with 2 : 4-dinitrophenylhydrazine.

Experimental.—Preparation of 6 : 6-*dialkyl- and* 6 : 6-*diaryl-naphtho*(2′ : 1′-2 : 3)*pyrans.*[6] The benzocoumarin (0·077 mole) in dry benzene (250 c.c.) was added in 1½ hr. to a stirred Grignard solution from alkyl or aryl iodide (0·2 mole), magnesium (0·2 g.-atom), and ether (75 c.c.). The solution was refluxed for 1 hr. and set aside overnight. Decomposition with 22% ammonium chloride solution (300 c.c.) and extraction with ether gave an ethereal solution, which was washed with water and dried (Na_2SO_4). The alcohol was cyclised by refluxing glacial acetic acid (50 c.c.) for ½ hr., and the solution poured into water, and extracted with ether. The ethereal solution was washed with dilute sodium hydroxide solution, then water, and dried (Na_2SO_4). Removal of the solvent and distillation gave the naphthopyran.

6 : 6-*Dimethylnaphtho*(2′ : 1′-2 : 3)*pyran* (I*a*) (from 5 : 6-benzocoumarin [7]), b. p. 164°/3 mm. (75%), on crystallisation from dilute acetic acid, gave plates, m. p. 45° (Found: C, 85·5; H, 6·2. $C_{15}H_{14}O$ requires C, 85·7; H, 6·7%); it gave a picrate, red needles, m. p. 115°. The alcohol crystallised from methanol as needles, m. p. 130°.

The 6 : 6-*diethyl analogue* (Ic) (from 5 : 6-benzocoumarin [7]) had b. p. 180—182°/15 mm. (30%) (Found: C, 85·8; H, 7·4. $C_{17}H_{18}O$ requires C, 85·7; H, 7·6%).

6 : 6-Diphenylnaphtho(2′ : 1′-2 : 3)pyran (I*d*) (from 5 : 6-benzocoumarin [7,8]). After decomposition of the Grignard complex with ammonium chloride solution the product was steam-distilled and extracted with ether from the non-volatile portion. Removal of the solvent and crystallisation from ethanol afforded needles of the *pyran*, m. p. 159—160° (20%) (Found: C, 89·3; H, 5·4. $C_{25}H_{18}O$ requires C, 89·9; H, 5·4%).

The 4 : 6 : 6-*trimethyl analogue* (I*b*) (from 4-methyl-5 : 6-benzocoumarin), b. p. 188—190°/15 mm. (35%), crystallised from dilute acetic acid as plates, m. p. 74—76° (Found: C, 86·1; H, 7·2. $C_{16}H_{16}O$ requires C, 85·7; H, 7·1%).

[1] Livingstone and Whiting, *J.*, 1955, 3631.
[2] Livingstone and Watson, *J.*, 1957, 1509.
[3] Hendry, Sandrock, and Robertson, *J.*, 1931, 2426.
[4] Cavill, Dean, McGookin, Marshall, and Robertson, *J.*, 1954, 4573.
[5] Arima, *J. Chem. Soc. Japan*, 1932, **53**, 715.
[6] Smith and Ruoff, *J. Amer. Chem. Soc.*, 1940, **62**, 145.
[7] Kauffman, *Ber.*, 1883, **16**, 685; Boehm and Profft, *Ann. Chim.*, 1931, 16.
[8] Löwenbein, *Ber.*, 1924, **57**, 1517.

Preparation of dimethylnaphthopyran dimers. The dimethylnaphthopyran (0·01 mole) was boiled with formic acid (75 c.c.; *d* 1·2) for 2 hr. The mixture was cooled, and the precipitate separated by filtration, washed with sodium hydrogen carbonate solution, then water, and dried. The dimer was recrystallised from a suitable solvent.

(*a*) *The* 6 : 6-*dimethylnaphtho*(2′ : 1′-2 : 3)*pyran dimer*, crystallised from ethyl acetate, had m. p. 204° (50%) [Found: C, 85·7; H, 6·6%; *M*, 433. $(C_{15}H_{14}O)_2$ requires C, 85·7; H, 6·8%; *M*, 420].

(*b*) *The* 6 : 6-*dimethylnaphtho*(1′ : 2′-2 : 3)*pyran dimer* crystallised as plates (from ethanol), m. p. 132—134° (Found: C, 85·9; H, 6·9%; *M*, 395).

6 : 6-*Dimethylnaphtho*(2′ : 1′-2 : 3)*pyran* 2 : 4-*dinitrophenylhydrazine derivative*. The naphthopyran (1 mol.), 2 : 4-dinitrophenylhydrazine (2·2 mols.), butan-1-ol (3·5 l./mole), and sulphuric acid (0·38 l./mole) were refluxed for 3 hr. The residue afforded by the removal of the solvent and excess of hydrazine was purified by chromatography on alumina from benzene. The derivative, recrystallised from glacial acetic acid, had m. p. 254° alone or mixed with 2 : 2-dimethyl-5 : 6-benzochroman-4-one 2 : 4-dinitrophenylhydrazone.

2 : 2-*Dimethyl*-5 : 6-*benzochroman*-4-*one*. ββ-Dimethylacryloyl chloride (3·6 g.) was added to a solution of 2-naphthol (4 g.) in nitrobenzene (31 c.c.). Anhydrous aluminium chloride (3·8 g.) was added in small portions to the cooled solution, and the mixture set aside for 12 days.[6] The mixture was poured on ice and 3N-hydrochloric acid, the nitrobenzene removed by steam-distillation, and the residue extracted with ether. The ethereal extract was washed with dilute sodium hydroxide solution and water. Evaporation of the dried ($MgSO_4$) extract gave a brown oil (2·8 g.) which was chromatographed on alumina from benzene solution. Removal of the solvent and crystallisation from light petroleum (b. p. 40—60°) afforded 2 : 2-*dimethyl*-5 : 6-*benzochroman*-4-*one* as prisms, m. p. 81° (Found: C, 79·7; H, 6·4. $C_{15}H_{14}O_2$ requires C, 79·65; H, 6·2%).

The crude dinitrophenylhydrazone, obtained by treating a warm ethanolic solution of the chroman-4-one with an excess of Brady's reagent, was purified by chromatography on alumina from benzene. Crystallisation from benzene afforded crimson plates, m. p. 254°.

Two of the authors (D. M. and R. B. W.) thank Burnley Education Authority for financial assistance.

MUNICIPAL COLLEGE, BURNLEY. [*Received, January 13th*, 1958.]

---

486. *Reactions of Amino-acids with Acetic Acid.*

By E. A. BELL.

AMINO-ACIDS with acetic anhydride [1] and keten [2] have given optically active acetamido-acids, racemic acetamido-acids, oxazolones, and acetamidoacetone derivatives, depending on the amino-acid,[3] the choice and concentration of acetylating agent, the temperature,[4] and the pH [5] at which the reaction is carried out.

As briefly reported,[6] ornithine and citrulline have been converted into 3-acetamido-2-piperidone by refluxing acetic acid. The ease with which these reactions proceed suggested that other amino-acids might be readily acetylated under the same conditions. Leucine, valine, alanine, and α-aminobutyric and α-amino-α-methylpropionic acid have now been found to be acetylated smoothly and in good yield in this way. However, glutamic acid is dehydrated rapidly to 5-oxopyrrolidine-2-carboxylic acid, and ornithine and citrulline undergo both acetylation and dehydration.

[1] Bergmann and Zervas, *Biochem. Z.*, 1928, **203**, 280.
[2] Bergmann and Stern, *Ber.*, 1930, **63**, 437.
[3] Wolff and Berger, *J. Amer. Chem. Soc.*, 1951, **73**, 3533; du Vigneau and Meyer, *J. Biol. Chem.*, 1932, **98**, 295.
[4] Neuberger, *Biochem. J.*, 1938, **32**, 1452; Dakin and West, *J. Biol. Chem.*, 1928, **78**, 745.
[5] Jackson and Cahill, *ibid.*, 1938, **126**, 37; Cahill and Burton, *ibid.*, 1940, **132**, 161.
[6] Bell, *Chem. and Ind.*, 1956, 1143.

XUM

Optically active alanine, valine, leucine, and glutamic acid as well as the racemic forms were refluxed with acetic acid; racemic derivatives were obtained in every case.

Glutamic acid was refluxed with butan-1-ol to establish that its rapid dehydration by boiling acetic acid is not merely a temperature effect (butanol was chosen because of its similarity to acetic acid in respect of its boiling point and its properties as a solvent for 5-oxopyrrolidine-2-carboxylic and glutamic acid—the former is readily soluble in both liquids, and the latter in neither). 5-Oxopyrrolidine-2-carboxylic acid was formed under these conditions, but only in low yield and after prolonged refluxing.

Experimental.—In each of the following reactions the amino-acid was refluxed in the free state with acetic acid. The excess of acetic acid and water were then distilled off under reduced pressure and the product was recrystallised.

Comparison of R_F values was carried out by downward chromatography on paper (Whatman No. 1) in phenol–water (4 : 1 w/v). Whatman No. 3 MM. paper, phosphate buffer (pH 8), and 2·5—5 v/cm. were used for ionophoresis.

TABLE 1. *Dehydration of glutamic acid.*

No.	Acid	Refluxed with	Time (hr.)	Yield (%)	M. p.	$[\alpha]_D^{20}$ (in H_2O)
1	DL	AcOH	20	100	178—180°	0
2	L	,,	2	68	175—177	0
3	DL	BuOH	20	9	174—176	0

		Found (%)			Calculated (%)			Acid equiv.	
No.		C	H	N	C	H	N	Found	Calc.
1	$C_5H_7O_3N$	46·4	5·34	10·9	46·5	5·43	10·9	128	129
2	,,	46·5	5·33	10·7	,,	,,	,,	127	,,

Anderlini [9] gives m. p. 176—180° for racemic 4-oxopyrrolidine-2-carboxylic acid, and Menozzi and Appiani [10] give m. p. 159—160° and $[\alpha]_D^{25}$ −7·2° (in H_2O) for the *lævo*-isomer.

TABLE 2. *Acetylation of amino-acids.*

No.	Amino-acid	Reflux time (hr.)	Yield (%)	M. p.	M. p. (lit.) [a]
1	DL-Valine	20	74	145—146°	144—146° [a]
2	L-Valine	22	74	144—145	,,
3	DL-Alanine	8	44	134—136	136 [a]
4	L-Alanine	22	61	134—136	,,
5	DL-Leucine	20	75	156—158	155—157 [b]
6	L-Leucine	22	75	154—156	,,
7	DL-Norleucine	20	87	106	104·5—105·5 [b]
8	DL-α-Aminobutyric	20	90	128—130	129—131 [c]
9	α-Amino-α-methylpropionic	20	21	191	195—196 [c]

		Found (%)			Calculated (%)			Acid equiv.	
No.		C	H	N	C	H	N	Found	Calc.
1	$C_7H_{13}O_3N$	52·92	8·31	8·9	52·84	8·2	8·8	160	159
3	$C_5H_9O_3N$	45·65	6·99	10·9	45·8	6·87	10·7	132	131
5	$C_8H_{15}O_3N$	55·38	8·7	8·2	55·5	8·68	8·2	173	173
7	,,	55·48	9·02	8·4	,,	,,	,,	172	,,
8	$C_6H_{11}O_3N$	49·27	7·44	10·1	49·6	7·58	9·65	145	145
9	,,	49·6	7·67	9·79	,,	,,	,,	148	,,

[*] The m. p. values from the literature are for the DL-acetamido-acids. The values for the relevant optically active acids are acetyl-L-valine, m. p. 157—158°, $[\alpha]_D^{20}$ +5·8 (in EtOH),[a] acetyl-L-alanine, m. p. 116°, $[\alpha]_D^{16}$ −45·6 (in H_2O) (Karrer, Escher, and Widmer, *Helv. Chim. Acta*, 1929, **9**, 301), acetyl-L-leucine, m. p. 167°, $[\alpha]_D^{16}$ −12·1 (in EtOH) (*idem, ibid.*). Determinations of [α] on products 2, 4, and 6 were carried out in the appropriate solvents.

[a] Synge, *Biochem. J.*, 1939, **33**, 1913. [b] Synder, Shekleton, and Lewis, *J. Amer. Chem. Soc.*, 1945, **67**, 310. [c] Levene and Steiger, *J. Biol. Chem.*, 1931, **93**, 581.

3-*Acetamido*-2-*piperidone*. DL-Ornithine (1·2 g.) was refluxed with acetic acid (100 ml.) for 13 hr. The product was obtained from aqueous acetone in needles (0·9 g.), m. p. 185—186°

alone or mixed with 3-acetamido-2-piperidone prepared from triacetylanhydro-DL-arginine [7] (Found: C, 54·1; H, 7·7; N, 17·5. Calc. for $C_7H_{12}O_2N_2$: C, 53·8; H, 7·7; N, 17·9%). Hydrolysis for 3 hr. at 100° with 20% hydrochloric acid regenerated DL-ornithine.

5-Oxopyrrolidine-2-carboxylic acid. (*a*) DL-Glutamic acid (2·0 g.) was refluxed with acetic acid (100 ml.) and in a second experiment with butan-1-ol (100 ml.). (*b*) L-Glutamic acid (2·0 g.) was refluxed with acetic acid (100 ml.).

The results of these three experiments are set out in Table 1. The identity of each product with authentic acid (prepared by the method of Abderhalden and Kautzsch [8]) was confirmed by chromatography, ionophoresis, and mixed m. p. The spots of acid on the dried chromatography and ionophoresis papers were developed by exposure to iodine vapour.

Acetyl-DL-amino-acids. Each amino-acid was refluxed in the free state with acetic acid (50 ml./g.), and the product recrystallised from ethanol. The results are set out in Table 2.

The derivatives of the three optically active amino-acids were not analysed as they showed no optical activity and no depression of m. p. when mixed with the acetyl derivatives of the corresponding racemic amino-acids.

The author thanks Professor W. Robson for his interest and for his many helpful suggestions

THE DEPARTMENT OF BIOCHEMISTRY,
KING'S COLLEGE, LONDON. [*Received, January 23rd,* 1958.]

[7] Bergmann and Koster, *Z. physiol. Chem.*, 1926, **159**, 179.
[8] Abderhalden and Kautzsch, *ibid.*, 1910, **68**, 487.
[9] Anderlini, *Gazzetta*, 1889, **19**, 100.
[10] Menozzi and Appiani, *ibid.*, 1894, **24**, I, 370.

487. *The Oxyfluorides of Manganese and Iodine.*

By E. E. AYNSLEY.

PURE manganese trioxyfluoride (permanganyl fluoride, MnO_3F) was prepared by Engelbrecht and Grosse [1] from potassium permanganate and fluorosulphuric acid and Aynsley, Nichols, and Robinson,[2] using iodine pentoxide and iodine pentafluoride, succeeded in isolating iodine oxytrifluoride IOF_3 and iodyl fluoride IO_2F. This communication describes the preparation of all three oxyfluorides by the reaction of potassium permanganate with excess of iodine pentafluoride. The reactions involved are:

$$KMnO_4 + IF_5 = MnO_3F + IOF_3 + KF$$
$$2IOF_3 = IO_2F + IF_5$$

In the preparation iodine pentafluoride must always be in large excess, otherwise there is the risk of a violent explosion when the temperature is raised to about 60°.

Experimental.—Preparation of manganese trioxyfluoride. About 50 ml. of iodine pentafluoride, prepared by burning dry iodine in a fluorine–nitrogen stream (4 : 6, by vol.), was fractionated in a vacuum to free it from fluorine and iodine heptafluoride, and was then poured under the same conditions, on 5 g. of finely powdered potassium permanganate. No change was observed at room temperature but at *ca.* 40° reaction occurred and the permanganate rapidly dissolved to form a deep green solution. When the temperature was gradually raised further, green gaseous manganese trioxyfluoride was rapidly evolved: it was condensed into a trap cooled to −80°. Since manganese trioxyfluoride begins to decompose at 0°, there was appreciable evolution of oxygen and deposition of a brown mixture of the dioxide and difluoride of manganese on the walls of the reaction vessel. To complete the separation of manganese trioxyfluoride from its decomposition products and from a small amount of iodine pentafluoride, the crude oxyfluoride was distilled into a trap containing pellets of anhydrous potassium fluoride and for final purification the product was redistilled three times and collected as dark green crystals at −80° (Found: Mn, 44·9; F, 15·4. Calc. for MnO_3F: Mn, 45·1; F, 15·6%). The product had m. p. −38·2° in good agreement with that given by Engelbrecht and Grosse.[1]

[1] Engelbrecht and Grosse, *J. Amer. Chem. Soc.*, 1954, **76**, 2042.
[2] Aynsley, Nichols, and Robinson, *J.*, 1953, 623.

Near the entrance to the first of the three traps used in the final distillation there collected a small amount of a brown solid which contained manganese and fluorine but was not manganese difluoride (cf. Engelbrecht and Grosse [1]). The yield of this substance was too small to allow it to be identified with certainty but the author regards it as manganese trifluoride.

Preparation of iodine oxytrifluoride. The brown liquid left in the reaction vessel consisted of unchanged iodine pentafluoride containing dissolved iodine oxytrifluoride, mixed with potassium fluoride and the dioxide and difluoride of manganese. This liquid was filtered through a fritted-glass filter and the filtrate was evaporated to dryness, leaving crude iodine oxytrifluoride. This recrystallised from fresh boiling iodine pentafluoride as white needles from which the mother-liquor was removed by decantation, and the excess of iodine pentafluoride by evaporation under a vacuum at room temperature for 1 hr. (Found: I, 63·9; F, 28·2. Calc. for IOF_3: I, 63·6; F, 28·5%).

Preparation of iodyl fluoride. Iodine oxytrifluoride was heated to 110° in a stream of dry nitrogen. The crystals fell to a white powder, and elsewhere in the apparatus iodine pentafluoride collected. To remove the last traces of the latter, the solid was kept at 110°, the vessel being subjected to continuous exhaustion for 1 hr. The residue of iodyl fluoride was a fine white powder (Found: I, 71·5; F, 10·5. Calc. for IO_2F: I, 71·3; F, 10·7%).

Analytical methods. Manganese trioxyfluoride was first hydrolysed with water in a Polythene flask to permanganic acid and hydrogen fluoride, and the manganese determined by titrating the resulting solution with standard potassium oxalate solution. The oxyfluorides of iodine were decomposed by water to iodic acid and hydrogen fluoride. The iodine was then determined by acidification, addition of potassium iodide, and titration of the liberated iodine with standard sodium thiosulphate solution. Fluorine was determined by the methods of Willard and Winter [3] and Offerman [4] and as lead chlorofluoride.

CHEMISTRY DEPARTMENT, KING'S COLLEGE,
NEWCASTLE UPON TYNE, 1. [*Received, January 28th.* 1958.]

[3] Willard and Winter, *Ind. Eng. Chem. Analyt.*, 1933, **5**, 7.
[4] Offerman, *Z. angew. Chem.*, 1890, **3**, 615; cf. Adolph, *J. Amer. Chem. Soc.*, 1915, **37**, 2500.

---

488. *5-Nitro- and 5-Amino-2-benzylbenziminazole.*

By B. N. FEITELSON and R. ROTHSTEIN.

2-BENZYL-4 : 5-DIHYDROGLYOXALINE (I), theophylline, 8-benzyltheophylline, and 5-nitro- (II; X = NO_2) and 5-amino-2 : 3-dialkylindoles (II; X = NH_2) are known [1] to be capable of preventing the rise in blood-pressure normally obtained on introduction of a vasoconstrictor in dogs. It appeared of interest therefore to examine the effect on blood-pressure of the benziminazole analogue (III; X = H) of compound (I), and of 2-benzyl-5-nitro- (III; X = NO_2) and 5-amino-2-benzyl-benziminazole (III; X = NH_2), which show certain structural similarities with the above-mentioned theophylline and indole derivatives.

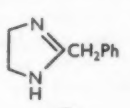
2-Benzyl-5-nitrobenziminazole (III; X = NO_2) was prepared by addition of nitric–sulphuric acid to a sulphuric acid solution of 2-benzylbenziminazole. Potassium nitrate in sulphuric acid failed to effect nitration, whereas the addition of a nitric acid suspension of 2-benzylbenziminazole to sulphuric acid, as in Bamberger's preparation [2] of 5-nitrobenziminazole, gave a benzyldinitrobenziminazole. The orientation of the nitro-group in the product (III) was confirmed by the identity of this substance with that obtained by synthesis, albeit in low yield, from 4-nitro-*o*-phenylenediamine and phenylacetic acid. Catalytic hydrogenation in the presence of Raney nickel provided the corresponding amine (III; X = NH_2).

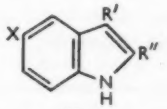
The dinitration product is 5-nitro-2-*p*-nitrobenzylbenziminazole since it is also obtained from 4-nitro-*o*-phenylenediamine and *p*-nitrophenylacetic acid. It is noteworthy that this reaction proceded more smoothly and in higher yield than that with phenylacetic acid.

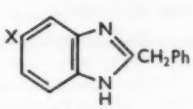
[1] Hager, Krantz, and Harmon, *J. Amer. Pharm. Assoc.*, 1953, **42**, 36; Shaw and Woolley, *J. Amer. Chem. Soc.*, 1952, **74**, 2948; 1953, **75**, 1877.
[2] Bamberger, *Annalen*, 1893, **273**, 303.

The same 5-nitro-2-*p*-nitrobenzylbenziminazole was also obtained by nitration of 2-4'-nitrobenzylbenziminazole.

Preliminary biological examination indicated that 5-amino-2-benzylbenziminazole (III; X = NH_2) caused a greater depression of arterial blood-pressure than the unsubstituted


(I)


(II)


(III)

compound (III; X = H) when administered intravenously in rabbits, whilst the 5-nitro-derivative (III; X = NO_2) proved too sparingly soluble for examination by this route.

Experimental.—*2-Benzylbenziminazole.* *o*-Phenylenediamine (5·4 g.), phenylacetic acid (6·8 g.), and 4N-hydrochloric acid (100 ml.) were heated under reflux for 7 hr. The mixture was cooled and made alkaline, and the precipitated solids were collected. The product recrystallised from benzene as needles (8·1 g., 72%), m. p. 187°. *2-Benzylbenziminazole hydrochloride* formed needles (from dilute hydrochloric acid), m. p. 175° (Found: Cl, 14·7. $C_{14}H_{13}N_2Cl$ requires Cl, 14·5%).

2-Benzyl-5-nitrobenziminazole. (*a*) To 2-benzylbenziminazole (5·7 g.), dissolved in concentrated sulphuric acid (50 ml.) at 0°, was added dropwise, with cooling and stirring, a mixture of concentrated nitric acid (1·6 ml.) and concentrated sulphuric acid (2·3 ml.) and stirring was continued for 1 hr. The mixture was poured on crushed ice, and the precipitated sticky solid was collected. This was taken up in ethanol, the solvent removed, and the residue, dissolved in anhydrous ethanol, neutralised with alcoholic sodium hydroxide. After removal of mineral salts, the solution was saturated with hydrogen chloride. On cooling, the solution deposited 2-benzyl-5-nitrobenziminazole hydrochloride (3·1 g.), m. p. 186—188°. Recrystallisation from 80 volumes of absolute alcohol yielded needles (2·5 g.), m. p. 191°.

(*b*) 4-Nitro-*o*-phenylenediamine (5·1 g.), phenylacetic acid (4·6 g.), and 4N-hydrochloric acid (50 ml.) were heated under reflux for 5 hr. The dark solids (5·2 g.) which had separated were removed and the filtrate was heated under reflux for 6 hr., whereafter a further quantity of product (1·6 g.) was removed. The combined solids (6·8 g.) were purified by dissolution in 20% sodium hydroxide solution and precipitation by mineral acid. This operation was repeated and the product recrystallised twice from aqueous ethanol, to give a small quantity of *2-benzyl-5-nitrobenziminazole*, white needles, m. p. 184° (Found: C, 65·9; H, 4·4; N, 17·2. $C_{14}H_{11}O_2N_3$ requires C, 66·4; H, 4·4; N, 16·2%). *The hydrochloride*, needles (from alcohol), had m. p. 192° alone or in admixture with the specimen obtained by nitration (Found: Cl, 11·9. $C_{14}H_{12}O_2N_3Cl$ requires Cl, 12·2%).

5-Amino-2-benzylbenziminazole dihydrochloride. 2-Benzyl-5-nitrobenziminazole (0·86 g.) in ethanol (50 ml.) was hydrogenated in the presence of Raney nickel. After removal of the catalyst, the solution was taken to dryness, the residue dissolved in absolute ethanol (15 ml.) and the solution saturated with hydrogen chloride. The product (0·85 g.), m. p. 206—207°, which separated, was collected and recrystallised from methanol, to yield *5-amino-2-benzylbenziminazole dihydrochloride* (0·65 g.), m. p. 207° (Found: C, 56·8; H, 5·2; N, 13·6. $C_{14}H_{15}N_3Cl_2$ requires C, 56·7; H, 5·1; N, 14·2%).

5-Nitro-2-p-nitrobenzylbenziminazole. (*a*) A mixture of 2-benzylbenziminazole (5 g.) and nitric acid (*d* 1·41; 20 ml.) was added portionwise, with stirring and cooling in ice–salt, to concentrated sulphuric acid (20 ml.). Stirring was continued for 1 hr., the mixture was poured on crushed ice, and the precipitated solids were collected. The dried material was taken up in hot absolute alcohol and neutralised by alcoholic sodium hydroxide, and the filtrate concentrated to small volume. On cooling, a yellow crystalline *product* (2·8 g.), m. p. 219—220°, was obtained. After 3 recrystallisations from alcohol the m. p. rose to 227—228° (Found: C, 56·6; H, 3·4; N, 18·8; O, 21·4. $C_{14}H_{10}O_4N_4$ requires C, 56·4; H, 3·4; N, 18·8; O, 21·4%) No hydrochloride could be obtained from this product.

(*b*) 4-Nitro-*o*-phenylenediamine (7·6 g.), *p*-nitrophenylacetic acid[3] (9 g.), and 4N-hydrochloric acid (90 ml.) were heated under reflux for 24 hr. and left overnight. The resulting

[3] Vogel, "Practical Organic Chemistry," Longmans, 1951, p. 723.

crystals were collected, washed with water, ground with sodium carbonate solution to remove unchanged acid, and dried, to give 11 g. of product, m. p. 219°. Recrystallisation from alcohol yielded 2-benzyl-4′ : 5-dinitrobenziminazole (7·8 g.), m. p. 227—228°, alone or in admixture with the product described above. The acid mother-liquors, on neutralisation, yielded unchanged diamine (2·3 g.), and from the alkaline extract of the crude product 4-nitrophenylacetic acid (2·3 g.) was recovered.

INSTITUT DE SEROTHERAPIE HEMOPOIETIQUE, PARIS (6e). [*Received, January 30th*, 1958.]

---

489. m-*Hydrazinostyrene.*

By C. L. ARCUS and R. E. SCHAFFER.

IN an investigation of the reactivity of groups attached to macromolecules [1] a monomer was required containing the hydrazino-group and the vinyl group; *m*-hydrazinostyrene has therefore been prepared.

m-Nitrostyrene is stated to be formed from *m*-nitrocinnamic acid, quinoline, and copper powder in 55% yield,[2] but we obtained yields of only 14 and 15%. Accordingly, preparation by dehydration of α-methyl-*m*-nitrobenzyl alcohol was investigated. Boiling with acetic anhydride–sulphuric acid is reported by Smets and Reckers [3] to give a 70% yield of *m*-nitrostyrene. However, we found that: (*a*) such treatment, with subsequent dilution and washing with water, gave α-methyl-*m*-nitrobenzyl acetate in good yield; (*b*) direct distillation gave a little acetate, and a gum; and (*c*) use, as in (*a*), of acetic acid in place of the anhydride, yielded a mixture of acetate and unchanged alcohol.

Marvel and his co-workers [4] have prepared *m*-nitrostyrene in 25% yield by thrice heating α-methyl-*m*-nitrobenzyl alcohol with phosphoric oxide in benzene and distillation in steam. It is more satisfactory to heat the benzyl alcohol with excess of phosphoric acid for a short time at above 100°, a 45% yield of *m*-nitrostyrene being obtained.

m-Nitrostyrene has been reduced to *m*-aminostyrene by stannous chloride and hydrochloric acid [5] and by tin and hydrochloric acid (giving 41% yield); [6] Wiley and Smith,[7] who used zinc and hydrochloric acid, obtained 84% of a polymer of the hydrochloride.

Reduction by hydrazine hydrate and Raney nickel [8] gave a 12% yield and by stannous chloride and ethanolic hydrochloric acid a 48% yield, both of monomer.

Diazotisation of *m*-aminostyrene proceeded smoothly. Attempted reduction with sodium hydrogen sulphite gave sulphur-containing products (cf. ref. 9); however, reduction of the diazonium chloride solution with stannous chloride and hydrochloric acid gave *m*-hydrazinostyrene in 39% yield.

Experimental.—M. p.s are corrected.

m-Nitroacetophenone [10] (75 g.), reduced by Lund's method [11] with aluminium *iso*propoxide [from aluminium (6·3 g.) and propan-2-ol (256 ml.)], gave α-methyl-*m*-nitrobenzyl alcohol [44 g.; from benzene–light petroleum (b. p. 60—80°)], m. p. 62°, and further crops (17 g.), m. p. 59—61°.

Dehydration. (*a*) α-Methyl-*m*-nitrobenzyl alcohol (6·3 g.), acetic anhydride (25 ml.), and

[1] Arcus, *J.*, 1949, 2732; *J. Polymer Sci.*, 1952, **8**, 365.
[2] *Org. Synth.*, 1953, **33**, 62.
[3] Smets and Reckers, *Rec. Trav. chim.*, 1949, **68**, 983.
[4] Marvel, Overberger, Allen, and Saunders, *J. Amer. Chem. Soc.*, 1946, **68**, 736.
[5] Komppa, Dissertation, Helsingfors, 1893; Beilstein, Hauptwerk, **12**, 1187.
[6] Matsui, *J. Soc. Chem. Ind. Japan*, 1942, **45**, Suppl., 437; *Chem. Abs.*, 1950, **44**, 9187.
[7] Wiley and Smith, *J. Amer. Chem. Soc.*, 1948, **70**, 2295.
[8] Balcom and Furst, *ibid.*, 1953, **75**, 4334.
[9] Kharasch, May, and Mayo, *J. Org. Chem.*, 1938, **3**, 175; Kharasch, Schenk, and Mayo, *J. Amer. Chem. Soc.*, 1939, **61**, 3092.
[10] *Org. Synth.*, Coll. Vol. II, 1st Edn., p. 434; Morgan and Watson, *J. Soc. Chem. Ind.*, 1936, **55**, 29T.
[11] Lund, *Ber.*, 1937, **70**, 1520.

XUM

sulphuric acid (*d* 1·84; 15 drops) were refluxed for 10 min., and then poured into water (500 ml.); the oil which separated was extracted with ether, and the extract was washed with water, dried (K_2CO_3), and distilled. The product (5·2 g.), b. p. 176—180°/16 mm., on redistillation yielded *α-methyl-m-nitrobenzyl acetate*, b. p. 112·5—114·5°/0·8 mm., n_D^{25} 1·5260 (Found: C, 58·1; H, 5·4; N, 6·95. $C_{10}H_{11}O_4N$ requires C, 57·4; H, 5·3; N, 6·7%).

(*b*) α-Methyl-*m*-nitrobenzyl alcohol (5·00 g.) and phosphoric acid ("AnalaR"; *d* 1·74; 40 ml.) were heated with mechanical stirring to 125° (bath temp.) during 12 min. and kept at that temperature for 1 min. The mixture was poured into water (500 ml.), and the yellow oil which separated was extracted with benzene. The extract was washed with water, dried (K_2CO_3), and, after the addition of quinol (0·05 g.), distilled. The yield of *m*-nitrostyrene, n_D^{25} <1·5810, b. p. of main fraction 81°/1·2 mm., was 45%.

Reduction. *m*-Nitrostyrene (6·95 g.), hydrazine hydrate (5·8 g.), and ethanol (70 ml.) were heated for 1 hr. at 70°, Raney nickel (approx. 0·5 g.) being added at 30°, and then boiled for 10 min., a little more catalyst having been added to decompose excess of hydrazine. The mixture was filtered and evaporated, and a benzene solution of the product extracted with 1·5N-hydrochloric acid; the extract, together with aqueous washings, was made alkaline (3N-sodium hydroxide) and extracted with benzene. The extract was washed with brine, dried (K_2CO_3), and distilled. It yielded *m*-aminostyrene (0·67 g.; 12%), b. p. 68—72°/0·8 mm. (Found: C, 79·25; H, 7·7; N, 11·85. Calc. for C_8H_9N: C, 80·6; H, 7·6; N, 11·75%).

m-Nitrostyrene (7·65 g.), stannous chloride dihydrate (46 g.), concentrated hydrochloric acid (46 ml.), and ethanol (23 ml.) were refluxed for 15 min., cooled, then poured into aqueous sodium hydroxide (68 g. in 230 ml.). The oil which separated from the steam-distillate was extracted with benzene, the extract was dried (K_2CO_3), and the benzene distilled after the addition of a little quinol; distillation of the product under oxygen-free nitrogen gave *m*-aminostyrene (2·93 g.; 48%), b. p. 68°/0·8 mm.

To *m*-aminostyrene (3·04 g.) hydrochloric acid (*d* 1·18; 31 ml.) was added at <0°; to the resulting slurry sodium nitrite (1·81 g.) in water (14 ml.) was added dropwise at <3°. After 5 min. stannous chloride dihydrate (11·5 g.) in hydrochloric acid (10 ml.) was added dropwise at 0—2°, and, after a further 10 min., the tin double salt was collected and dissolved in water (50 ml.) at 35°. The solution was poured into aqueous sodium hydroxide (8 g. in 40 ml.) in the presence of benzene (30 ml.) at 0°. The mixture was shaken, then separated and the aqueous layer further extracted. The combined extracts were washed once with water and dried (Na_2SO_4), and after the addition of quinol (15 mg.) the benzene was distilled off. The product, on distillation under oxygen-free nitrogen, yielded m-*hydrazinostyrene* (1·32 g.), b. p. 104—105°/0·3 mm., n_D^{25} 1·6200 (Found: C, 69·75; H, 7·4; N, 19·45. $C_8H_{10}N_2$ requires C, 71·65; H, 7·5; N, 20·9%). It (0·55 g.) was dissolved in aqueous acetic acid containing sodium acetate, and benzaldehyde (0·44 g.) in ethanol was added; the whole was heated on a steam-bath for 1 min., cooled, and filtered. The product (0·88 g.) gave *benzaldehyde* m-*vinylphenylhydrazone*, needles (from ethanol), m. p. 123·5° (Found: C, 81·1; H, 6·5; N, 12·2. $C_{15}H_{14}N_2$ requires C, 81·05; H, 6·35; N, 12·6%).

Thanks are expressed to Imperial Chemical Industries Limited for a grant.

BATTERSEA COLLEGE OF TECHNOLOGY, LONDON, S.W.11. [*Received, February 10th*, 1958.]

---

490. *Pyrolysis of Phenylmercuric Iodide.*

By M. COWPERTHWAITE and E. WARHURST.

CARTER, CHAPPELL, and WARHURST[1] showed that thermal decompositions of organomercury compounds fall into two classes. Class I is characterised by frequency factors in the "normal" range (*i.e.*, $A = 10^{13}$—10^{14} sec.$^{-1}$) and activation energies identifiable with values of the dissociation energy, D_1, of the first mercury–carbon bond. Dimethyl- and diethyl-mercury and phenylmercuric chloride and bromide are of this class. Class II is characterised by high frequency factors (10^{15}—10^{16} sec.$^{-1}$) and activation energies approximately equal to the sum of the first and second bond-dissociation energies (*i.e.*,

[1] Carter, Chappell, and Warhurst, *J.*, 1956, 106.

$D_1 + D_2$). Di-*n*- and di*iso*-propylmercury and diphenylmercury are of this class. These characteristics are suggested to arise from a difference in the nature of the first step in the thermal decomposition.[1,2,3] In members of class I only one bond is broken, producing two fragments, whereas in those of class II both bonds break simultaneously, giving three fragments.

There is little doubt that an essential requirement (though not the only one; see ref. 1) for class II behaviour is that D_2 should be small. Phenylmercuric iodide is an interesting and critical example for the classification since D_2 [*i.e.*, D(·Hg–I) = 8 ± 1 kcal. mole^{-1}] is very small and approximately equal to D_2 for the ·Hg·CH_3 and ·Hg·C_2H_5 radicals.

Experimental.—Materials. Phenylmercuric iodide, precipitated by adding an equimolar amount of B.D.H. diphenylmercury to red " AnalaR " mercuric iodide dissolved in hot acetone, was washed with chloroform and hot acetone and recrystallised (m. p. 271°) from hot acetone. The carrier gas, nitrogen, was purified as described by Morantz and Warhurst.[4] Toluene was purified as previously described.[1]

Apparatus and technique. As previously described,[1,5] a circulating stream of carrier gas introduces known partial pressures of toluene and substrate into a hot reaction vessel for known contact times. In the pyrolysis of phenylmercuric iodide all the substances issuing therefrom, except for a small fraction of the mercuric iodide, were condensed from the carrier gas stream in a U-tube at −80°. Determinations of the percentage decomposition were based on the amounts of undecomposed phenylmercuric iodide. Free mercury and mercurous iodide were removed as insoluble residues by treating the contents of the U-tube with hot acetone. Acetone and toluene were completely removed by careful evaporation. All remaining hydrocarbons were dissolved in the minimum of ice-cold carbon tetrachloride. Mercuric iodide was then removed as the soluble complex K_2HgI_4 by treatment with aqueous potassium iodide, leaving only undecomposed phenylmercuric iodide.

Results. Pyrolyses were done within the following range of conditions: total pressure = 8·5 ± 0·5 mm.; time of contact = 0·23—0·45 sec.; decomposition = 12—84%; toluene : PhHgI ratio = 19—43; toluene pressure = 3·0 ± 0·2 mm. Velocity constants were determined twice at 575°, twice at 598°, three times at 624°, and twice at 651°. They were calculated from $k = (1/\tau)\ \ln\ [100/(100 - f)]$, where τ is the time of contact (sec.) and f is the percentage decomposition. The activation energy obtained from the Arrhenius plot by the method of least squares is $E = 63 \pm 2$ kcal. mole^{-1} and the frequency factor $A = 10^{15\cdot7}$ sec.$^{-1}$. The average deviation from the least-squares line was 0·01, and the maximum deviation 0·03, in units of $\log_{10}k$. We estimate a limit of accuracy of ±2 kcal. mole^{-1} mainly from our general experience of this technique and the small number of experiments.

Discussion.—The determination of k from values of f from the amounts of undecomposed substrate is valid whatever the mechanism after the first dissociative step, provided that no free-radical intermediate reacts appreciably with the substrate. This seems very improbable because pyrolyses of phenylmercuric chloride and bromide and diphenylmercury, investigated in more detail than the present one, are free from such complications. Comparisons of estimates of the heats of likely reactions between radical intermediates and these four substrates indicate that such reactions should be even less likely in the phenylmercuric iodide system. We do not consider that there can be an appreciable hetergeneous contribution to the decomposition since pyrolyses of other mercury alkyls at temperatures *lower* than the one used here are predominantly homogeneous.

Our value of $10^{15\cdot7}$ sec.$^{-1}$ for the frequency factor for the decomposition of phenylmercuric iodide is large and lies in the class II range.[1] Our value for the activation energy, 63 ± 2 kcal. mole^{-1}, lies in the possible range of values for $D_1 + D_2$ obtained[6] from thermochemistry and spectroscopy [based on D(Ph–H) = 97·8: $D_1 + D_2 = 63{\cdot}2 \pm 3$;

[2] Chilton and Gowenlock, *Trans. Faraday Soc.*, 1953, **49**, 1451; 1954, **50**, 824.
[3] Pritchard, *J. Chem. Phys.*, 1956, **25**, 267.
[4] Morantz and Warhurst, *Trans. Faraday Soc.*, 1955, **51**, 1375.
[5] Gowenlock, Polanyi, and Warhurst, *Proc. Roy. Soc.*, 1953, *A*, **218**, 269.
[6] Pritchard, Ph.D. Thesis, Manchester, 1951.

XUM

$D_2 = 8 \pm 1$; $D_1 = 55{\cdot}2 \pm 4$: based on $D(\text{Ph–H}) = 102$; $D_1 + D_2 = 67{\cdot}4 \pm 3$; $D_2 = 8 \pm 1$; $D_1 = 59{\cdot}4 \pm 4$ kcal. mole^{-1}], so we conclude that this compound is a genuine member of class II.

It appears that the interdependence of the extension energies of the Hg–Ph and Hg–I bonds of the molecule is such that the potential-energy surface for the various nuclear configurations possesses a pronounced "diagonal basin" (ref. 1). Consequently the most probable mode of decomposition is that corresponding to simultaneous stretching of both bonds yielding three fragments in a single step. The very low value of D_2 contributes to this effect.

MANCHESTER UNIVERSITY. [*Received, February 11th*, 1958.]

---

491. *The C-Benzylation of Phenols by Use of Sodium Hydride.*

By F. M. ELKOBAISI and W. J. HICKINBOTTOM.

IT is known that a benzyl group can be introduced directly into the *ortho*-position of a phenol by reaction of a suspension of its sodium salt in benzene or toluene with benzyl chloride.[a] In the course of other work, it was observed that the suspension of the sodium salt can be obtained more cleanly and conveniently if sodium hydride, suspended in toluene, was used instead of sodium as described by Claisen.

EXPERIMENTAL

The following general conditions were found to be satisfactory. The phenol (1 mole) diluted with specially dried toluene (200 c.c.) was added dropwise to a warmed and stirred suspension of finely powdered sodium hydride (1 mole) in toluene. The addition of the phenol required about 1 hr. and the reaction was completed by stirring and heating the mixture under reflux for another hour. The result was a thick pasty suspension of the sodium salt of the phenol.

To this suspension, benzyl chloride (1 mole), diluted with some toluene, was added steadily. With *ortho*-substituted phenols, it was more satisfactory to use 1·2—1·3 moles of benzyl chloride. As the reaction proceeded, the suspension became thinner owing to the formation of sodium chloride; it was completed by 2 hours' heating under reflux after all the chloride had been

Substituted phenol	B. p./mm.	M. p.	Found (%) C	H	Formula	Calc. (%) C	H	Derivative, m. p.
2-Benzyl [a]	170°/15	—	84·8	6·5	$C_{13}H_{12}O$	84·7	6·6	Phenylurethane, 117°
2 : 4-Dibenzyl [b]	260°/15	48—49°	87·1	6·7	$C_{20}H_{18}O$	87·6	6·6	α-Naphthylurethane, 148—149°
2 : 6-Dibenzyl [c]	240°/15	—	87·6	6·5	$C_{20}H_{18}O$	87·6	6·6	α-Naphthylurethane, 168°
2-Benzyl-6-methyl [d]	143°/1	52	84·5	7·1	$C_{14}H_{14}O$	84·8	7·1	*p*-Bromo-compound, 66°
2-Benzyl-4-methyl [e]	186°/15	36	84·8	7·4	$C_{14}H_{14}O$	84·8	7·1	Phenylurethane, 146°
2-Benzyl-4-chloro	204°/15	53	71·4 Cl, 16·2	5·0	$C_{13}H_{11}OCl$	71·4 Cl, 16·2	5·0	Phenylurethane, 165°

[a] Claisen (*Annalen*, 1925, **442**, 238) gives m. p. 21°, b. p. 171°/13 mm. (phenylurethane, m. p. 117·5—118°). [b] Prepared from *p*-benzylphenol. Short and Stewart (*J.*, 1929, 558) give for 2 : 4-dibenzylphenol, b. p. 252—254°/10 mm. (α-naphthylurethane, m. p. 144°). [c] Prepared from *o*-benzylphenol. Short and Stewart (*loc. cit.*) give for 2 : 6-dibenzylphenol, b. p. 237·5—238°/10 mm. (α-naphthylurethane, m. p. 165—166°). [d] Schorigin (*Ber.*, 1925, **58**, 2033) gives b. p. 187—188°/15 mm., m. p. 51—52°; Huston, Swartout, and Wardwell (*J. Amer. Chem. Soc.*, 1930, **52**, 4484) give *p*-bromo-compound, m. p. 63—64°. [e] Claisen (*Annalen*, 1925, **442**, 241) gives b. p. 180—182°/12 mm. (phenylurethane, m. p. 144·5—145°); Huston and Lewis (*J. Amer. Chem. Soc.*, 1931, **53**, 2379) give m. p. 35—36°.

added and then storage overnight. The clear toluene solution was washed with water, dried, and distilled to remove solvent. The residual oil was dissolved in 5 times its volume of methyl-alcoholic potassium hydroxide (Claisen's solution) and freed from neutral matter by repeated

extractions with light petroleum. The residual alkaline solution was concentrated to remove alcohol, then acidified, and the phenols were taken up in ether.

The Table summarises the constants of phenols prepared in this way; the yields were generally 80—90%.

QUEEN MARY COLLEGE (UNIVERSITY OF LONDON),
MILE END ROAD, LONDON, E.1. [*Received, February* 12*th*, 1958.]

---

492. *Alkaloids of* Rauwolfia *Species. Part IV.*[1] Rauwolfia cambodiana *Pierre.*

By D. A. A. KIDD.

ALTHOUGH no detailed chemical study had been published, *Rauwolfia cambodiana*[2] was included by Maison[3] in a group reported to be free from reserpine. Since that alkaloid is an almost invariable constituent of *Rauwolfia* species, a quantity of *R. cambodiana* roots was extracted with methanol, subsequent fractionation of the extract being carried out by a method similar to that used by Hochstein, Murai, and Boegemann[4] for *R. heterophylla*.

The greater part of the alkaloids (3·4% of powdered root) separated in the weakly basic fraction, which was shown by paper electrophoresis to contain two major components. As already indicated[1] one of these is reserpine, which was isolated by chromatography and identified by direct comparison with an authentic specimen. The second, which gave a strongly fluorescent brownish-yellow spot and presumably corresponded to that described by Dillemann and Paris,[5] had properties (see Table) resembling those described for *iso*-reserpiline, already encounted in *R. canescens*,[6] *R. vomitoria*,[7] and *R. schueli*.[8] Some minor differences between the infrared spectra of the *cambodiana* alkaloid and that published for *iso*reserpiline[6] were evidently due to the different method of determination, since a direct comparison of its methanesulphonate with an authentic sample of *iso*reserpiline methanesulphonate established their identity.

From the mother-liquors of *iso*reserpiline, a third alkaloid was isolated as its di-*p*-toluoyl-L-tartrate but the quantity of free base obtained from it was too small for further identification.

The strongly basic fraction, of which unusually little was obtained, gave a complex electrophoresis pattern. A strongly fluorescing blue spot corresponding in mobility with that of serpentine was present, together with a strong greenish spot distinct from that of reserpine and five or six weaker spots. Spotting with concentrated nitric acid gave a red colour in the position expected for ajmaline; this alkaloid normally separates with the weaker bases but the persistence of traces in the strongly basic fraction has been previously noted with *R. sellowii*.

For pharmacological purposes, it was important to know more accurately the content of reserpine in *R. cambodiana*, and the method of isolation used was unsuitable for this purpose. The countercurrent distribution method[9] described for *R. serpentina* and *R. vomitoria* gave inadequate resolution between reserpine and *iso*reserpiline in the small number of transfers involved, and an alternative method of extraction was therefore adopted, which had earlier been found reliable for the quantitative isolation of reserpine

[1] Part III, *Chem. and Ind.*, 1957, 1013.
[2] Craib, *Florae Siamensis Enumeratio*, 1939, **2**, 428.
[3] Maison, *Lancet*, 1955, **268**, 866.
[4] Hochstein, Murai, and Boegemann, *J. Amer. Chem. Soc.*, 1955, **77**, 3551.
[5] Dillemann and Paris, *Compt. rend.*, 1957, **244**, 1254.
[6] Stoll, Hofmann, and Brunner, *Helv. Chim. Acta*, 1955, **38**, 270.
[7] Poisson and Goutarel, *Bull. Soc. chim. France*, 1956, 1703.
[8] Iacobucci and Deulofeu, *J. Org. Chem.*, 1957, **22**, 94.
[9] Kidd and Scott, *J. Pharm. Pharmacol.*, 1957, **9**, 176.

in other species. The content of reserpine in powdered whole *R. cambodiana* root containing 11% of moisture was 0·01%.

Experimental.—All melting points were determined in evacuated capillaries, and infrared spectra in potassium bromide discs.

Extraction. Finely ground roots (2 kg., containing 11% of moisture), collected during late summer in Bangkhen, Thailand, were percolated slowly with cold methanol (40 l.) and finally extracted with boiling methanol (15 l.). The combined extracts were evaporated *in vacuo* and the soft residue poured into 5% acetic acid (1 l.) to give a turbid mixture which was defatted with light petroleum and filtered through kieselguhr. The chilled filtrate was basified with ammonia (s.g. 0·88) below 10° and the bulky precipitate collected. Extraction of a small additional quantity from the liquor with chloroform gave a combined weakly basic fraction (68·25 g.; 3·4% on powdered root). Further basification of the aqueous phase with sodium hydroxide followed by chloroform extraction gave a strongly basic fraction (0·3 g.). The aqueous layer, after adjustment of pH, was treated with saturated ammonium reineckate solution and a reineckate fraction obtained (18·75 g.).

Purification of weak bases. A part (30 g.) of the weakly basic fraction was repeatedly extracted with cold chloroform, and the insoluble residue adsorbed on kieselguhr and then extracted with 1N-acetic acid. Evaporation of the chloroform extract gave fraction *A* (6·65 g.) and basification of the acid phase an amorphous precipitate [fraction *B* (12·6 g.)]. Paper electrophoresis in 3N-acetic acid (400 v) of fraction *B* gave only one, yellowish-brown fluorescent spot, which was also obtained from fraction *A* together with a yellowish-green spot corresponding to reserpine.

Chromatography of fraction *A* on alumina (150 g.) in benzene, elution with benzene–acetone (9 : 1), and crystallisation of the amorphous residues from methanol containing a little water, gave flat prisms of *iso*reserpiline, m. p. 211—212° (0·29 g.), $[\alpha]_D^{21}$ −111° (*c* = 2·1 in chloroform) (Found: N, 6·9. Calc. for $C_{33}H_{38}O_9N_2$: N, 6·8%).

Treatment of the mother-liquors with di-*p*-toluoyl-L-tartaric acid gave a crystalline di-*p*-toluoyl-L-tartrate, minute prisms (from aqueous methanol), m. p. 213° (decomp.) (Found: C, 63·6; H, 7·2; N, 4·7%). The free base had m. p. 226—227° and is so far unidentified. Pale mauve colours were obtained in the Keller and the Fröhde reaction.

Subsequent elution of the column with benzene–acetone (3 : 1) gave a small quantity of reserpine, m. p. and mixed m. p. 277—278°; its infrared spectra, electrophoretic mobility, and Fröhde colour reactions also agreed with those of authentic material.

Fraction *B* was insoluble in the usual chromatographic solvents and no crystalline substance could be isolated from it.

iso*Reserpiline methanesulphonate.* This salt, prepared in methanol, separated when ether was added to incipient turbidity and was recrystallised from the same solvent. The needles, which were dried at 100°/0·01 mm., had m. p. and mixed m. p. 294—295° (decomp.). This value is higher than that (282—284°) recorded by Stoll, Hofmann, and Brunner,[6] but the difference must be due to the conditions of measurement since the same value was obtained on the pure sample provided by Dr. Hofmann. Our sample had infrared and ultraviolet spectra indistinguishable from those of authentic material (Found: N, 5·2. Calc. for $C_{22}H_{28}O_5N_2.CH_3{\cdot}SO_3H$: N, 5·5%).

	M.p.	$[\alpha]_D$ in $CHCl_3$	$\lambda_{max.}$ (log *E*)
*iso*Reserpiline	211—212° [6,8]	−102°,[7] −112° [8]	229, 304 (4·56, 4·02) [6]
R. cambodiana Alkaloid	211—212°	−111°	230, 303 (4·59, 4·05)

Quantitative isolation of reserpine. Concentrated methanolic extract of powdered root (500 g.) was adsorbed on kieselguhr, washed with cold water (3 × 1 l.), and extracted with 15% acetic acid. The acid extract was repeatedly shaken with chloroform, the combined chloroform layers were washed with 10% aqueous sodium carbonate (100 ml.) and water and evaporated to dryness, and the residue (0·87 g.) chromatographed on alumina in benzene. Elution with benzene–chloroform (3 : 1) and crystallisation of the residues gave reserpine, m. p. 274—275°, $[\alpha]_D^{19}$ −122° (0·052 g., 0·01% yield on powdered root).

The author thanks Professor Kasin Suvatabandu of the Agricultural University of Bangkhen, Thailand, for collecting and identifying plant material, Dr. A. Hofmann of Sandoz A.G. for a

XUM

specimen of *iso*reserpiline methanesulphonate, and the Directors of May & Baker Ltd. for permission to publish this Note.

THE RESEARCH LABORATORIES, MAY & BAKER LTD.,
DAGENHAM, ESSEX. [*Received, February 13th*, 1958.]

---

493. *Trismethylmercurisulphonium Nitrate and Dichromate.*

By D. GRDENIĆ and B. MARKUŠIĆ.

IT was reported recently that trismethylmercurioxonium fluoroborate was obtained by neutralization of an alcoholic solution of methylmercuric hydroxide with fluoroboric acid,[1] and the reaction was interpreted [2] as addition of methylmercuric fluoroborate to methylmercuric oxide.[3] It was shown that methylmercuric hydroxide, prepared by Slotta and Jacobi's method, was a mixture of oxide and hydroxide, so that the pure oxide was obtained by dehydration of the crude material. This class of oxonium compounds can be prepared by addition:

$$(RHg)_2O + RHgX \longrightarrow [(RHg)_3O]X \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

or by partial neutralization:

$$3(RHg)_2O + 2HX \longrightarrow 2[(RHg)_3O]X + H_2O \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

The present note deals with the application of reaction (2) to the preparation of the sulphonium compounds. When a solution of bismethylmercuric sulphide in benzene is shaken with an aqueous solution of chromium(VI) oxide or potassium dichromate, yellow crystalline trismethylmercurisulphonium dichromate is deposited immediately and quantitatively. This is insoluble in benzene, ether, or chloroform, and scarcely soluble in

$$3(CH_3Hg)_2S + H_2Cr_2O_7 \longrightarrow [(CH_3Hg)_3S]_2Cr_2O_7 + H_2S \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

ethanol, but recrystallizes from water. Double decomposition with lead nitrate in ethanol gives the sulphonium nitrate which crystallizes in colourless needles. Both the nitrate and the dichromate are fairly stable except that they are slightly sensitive to light.

Bismethylmercuric sulphide was prepared previously [4] by the action of hydrogen sulphide on methylmercuric chloride in alcohol.[4] We found this method unsatisfactory and elaborated a convenient preparation by use of sodium sulphide.

Experimental.—Trismethylmercurisulphonium dichromate. An aqueous solution (40 ml.) of chromium(VI) oxide (1·6 g.) was added to a solution of bismethylmercuric sulphide (5 g.) in warm benzene (150 ml.) and the mixture shaken. The brownish-yellow *dichromate* was collected (filtrate I), washed with water, and recrystallized from boiling water (600 ml.; 4 or 5 times). The golden-yellow leaflets (5 g.) decompose at 200°, are stable in air but darken on exposure to light (Found: Hg, 76·7; Cr, 6·6; S, 3·9. $C_6H_{18}O_7S_2Cr_2Hg_6$ requires Hg, 76·7; Cr, 6·6; S, 4·0%). Solutions in cold and hot water give reactions for dichromate and chromate respectively.

The benzene component of the filtrate (I) contained insignificant quantities of sulphur and bismethylmercuric sulphide. The aqueous part did not contain mercury but gave the reaction for sulphate ion which resulted from the oxidation of hydrogen sulphide. According to the equation (3), each mol. of bismethylmercuric sulphide evolves 1/3 mol. of hydrogen sulphide, which on its turn uses 8/9 mol. of chromium(VI) oxide for complete oxidation to sulphuric acid. The corresponding quantity of chromium(III) ions was found by analysis in the remaining aqueous solution, so reaction (3) is established.

Trismethylmercurisulphonium nitrate. Trismethylmercurisulphonium dichromate (1·5 g.,

[1] Grdenić, XVIth Internat. Congr. Pure Appl. Chem., 1957, Congress Handbook, Vol. II, p. 112.
[2] Grdenić and Zado, *Croat. Chem. Acta*, 1957, **29**, 425.
[3] Slotta and Jacobi, *J. prakt. Chem.*, 1929, **120**, 249.
[4] Hilpert and Ditmar, *Ber.*, 1913, **46**, 3738; A. Perret and R. Perrot, *Helv. Chim. Acta*, 1933, **16**, 848.

XUM

1 mol.) and lead nitrate (0·32 g., 2 mol.) were moistened with a little ethanol and thoroughly mixed by means of a pestle and mortar (1 hr.). The yellow solid was collected and extracted (small Buchner funnel) with ethanol (60 ml.). The filtrate was evaporated *in vacuo*, the crystalline residue (1·2 g.) dissolved in ethanol, the solution filtered, and the filtrate treated with twice its volume of dry ether and cooled overnight. Colourless needles of the *nitrate* were formed, very soluble in water or ethanol, decomposing at 160° (Found: NO_3, 8·4; Hg, 81·1. $C_3H_9O_3NSHg_3$ requires NO_3, 8·4; Hg, 81·2%) (the nitrate ion was determined in aqueous solution by means of nitron acetate).

Bismethylmercuric sulphide. A warm solution of methylmercuric bromide (10 g.) in acetone (200 ml.) was divided into two equal parts. A solution of sodium sulphide (20 g. of nonahydrate in 250 ml. of ethanol) was added gradually to one part until the white precipitate just dissolved. To this solution, which apparently contains sodium methylmercuric sulphide, the second part of the methylmercuric bromide solution was added and the mixture cooled. The white crystalline precipitate of bismethylmercuric sulphide was collected (7·7 g.), and recrystallized from benzene (200 ml.) as leaflets, m. p. 144° (lit., 143°), becoming grey on long exposure to light.

We thank Institute "Rudjer Bošković," Zagreb, for experimental facilities, and M. M. Dadić for critical remarks.

LABORATORY FOR GENERAL AND INORGANIC CHEMISTRY, FACULTY OF SCIENCE,
UNIVERSITY, ZAGREB, YUGOSLAVIA. [*Received, February 17th*, 1958.]

---

494. *The Hunsdiecker Reaction in the Pyrazole Series.*

By E. G. BRAIN and I. L. FINAR.

IN an attempt to discover a relation between the orientation of pyrazolecarboxylic acids and their behaviour in the Hunsdiecker reaction ($R{\cdot}CO_2Ag + Br_2 \longrightarrow RBr + AgBr + CO_2$), several silver pyrazolecarboxylates were subjected to the action of anhydrous bromine in carbon tetrachloride. Silver 1-phenylpyrazole-4-carboxylate gave 4-bromo-1-phenylpyrazole with some 4-bromo-1-*p*-bromophenylpyrazole. The latter compound was shown to be the normal product of further bromination of 4-bromo-1-phenylpyrazole.[1]

Silver 4-bromo-1 : 3-dimethylpyrazole-5-carboxylate yielded 4 : 5-dibromo-1 : 3-dimethylpyrazole, but silver 4-bromo-1 : 5-dimethylpyrazole-3-carboxylate was unaffected by bromine under the same conditions. Two other pyrazole-3-carboxylates which were investigated also failed to give the Hunsdiecker reaction. Silver 1 : 4-dimethylpyrazole-3-carboxylate was unaffected by the reagent: silver 1 : 5-diphenylpyrazole-3-carboxylate was brominated to give silver 4-bromo-1 : 5-diphenylpyrazole-3-carboxylate, on which an excess of bromine had no further action.

From this limited number of experiments it appears that the carboxyl group in position 3 of the pyrazole nucleus is resistant to the Hunsdiecker reaction.

Experimental.—Bromine and carbon tetrachloride were dried over phosphoric oxide. Silver salts were precipitated from neutral aqueous solutions of the ammonium salts by the addition of silver nitrate solution. With one exception they were dried for several hours at 120°.

4-Bromo-1-phenylpyrazole. Silver 1-phenylpyrazole-4-carboxylate (4·35 g., 1 mol.) was suspended in boiling carbon tetrachloride (30 c.c.), and bromine (1 mol.) in carbon tetrachloride was slowly added. This was rapidly decolorised except for the last drops. The solution was then filtered from silver bromide, and the filtrate was washed with dilute aqueous ammonia, then with water; when dried (Na_2SO_4) and evaporated, this gave 4-bromo-1-phenylpyrazole[1] (2·0 g., 59%), m. p. 70—72°. Pure 4-bromo-1-phenylpyrazole (0·5 g., 15%) was obtained from this by chromatography on alumina with benzene–light petroleum and had m. p. and mixed m. p. 81·5—82·5°. No other compound was isolated by this method or by fractional crystallisation

[1] Balbiano, *Gazzetta*, 1889, **19**, 128.

XUM

from dilute ethanol. The infrared absorption spectrum of the crude product in CCl_4 and CS_2 showed bands due to both 4-bromo-1-phenylpyrazole and 4-bromo-1-*p*-bromophenylpyrazole.

4-Bromo-1-p-bromophenylpyrazole. 1-*p*-Bromophenylpyrazole was treated with 1 mol. of bromine in chloroform. The product, twice recrystallised from dilute ethanol, gave elongated platelets, m. p. 84·5—85°, identical with dibromo-1-phenylpyrazole obtained by brominating 4-bromo-1-phenylpyrazole [1] (mixed m. p.; infrared spectra).

4 : 5-Dibromo-1 : 3-dimethylpyrazole. Silver 4-bromo-1 : 3-dimethylpyrazole-5-carboxylate [2] was dried by washing it with dry methanol and then heating it at 60—70° for 3 hr. since it decomposed at 120°. When treated with bromine in the usual way the silver salt decolorised about 1 mol. of bromine. The mixture was worked up as for 4-bromo-1-phenylpyrazole but the residue on evaporation was an oil. Pure 4 : 5-*dibromo*-1 : 3-*dimethylpyrazole* was obtained by chromatography on alumina with light petroleum, and had m. p. 74—75° (50%) (Found: N, 10·8; Br, 63·2. $C_5H_6N_2Br_2$ requires N, 11·05; Br, 63·0%).

Action of bromine on silver 1 : 5-diphenylpyrazole-3-carboxylate. The silver salt was obtained from the acid [3] by the usual method, and when treated with bromine in carbon tetrachloride by the previous method gave no residue on evaporation of the filtrate. The reaction residue was boiled again with excess of bromine solution for 90 min. and again filtered off, etc. This filtrate also left no residue on evaporation. Free *4-bromo-1 : 5-diphenylpyrazole-3-carboxylic acid* was liberated from the insoluble reaction residue by refluxing it with 1 : 1 3N-hydrochloric acid–ethanol. The mixture was filtered, the filtrate evaporated, and after recrystallisation from dilute ethanol crystals, m. p. 221—222·5°, were obtained. The mixed m. p. with the bromo-acid (m. p. 223°) obtained by brominating 1 : 5-diphenylpyrazole-3-carboxylic acid in carbon tetrachloride was not depressed (Found: C, 56·3; H, 3·1; N, 8·3; Br, 23·3. $C_{16}H_{11}O_2N_2Br$ requires C, 56·0; H, 3·2; N, 8·2; Br, 23·3%).

Action of bromine on silver 4-bromo-1 : 5-dimethylpyrazole-3-carboxylate. [2] When this silver salt was treated with bromine under the usual conditions no decolorisation was observed after 6 hours' refluxing, and the filtrate left no residue on evaporation. A small amount of 4-bromo-1 : 5-dimethylpyrazole-3-carboxylic acid, m. p. and mixed m. p. 194°, was recovered from the silver salt by means of hydrochloric acid–ethanol.

Action of bromine on silver 1 : 4-dimethylpyrazole-3-carboxylate: 1 : 4-Dimethylpyrazole-3-carboxylic acid [4] was obtained by hypobromite oxidation of 3-acetyl-1 : 4-dimethylpyrazole.[5] The silver salt was treated by the usual method. No residue was obtained on evaporating the filtrate, and unchanged 1 : 4-dimethylpyrazole-3-carboxylic acid, m. p. and mixed m. p. 165—169°, was recovered from the silver salt.

One of us (E. G. B.) thanks the D.S.I.R. for a maintenance grant.

THE NORTHERN POLYTECHNIC, HOLLOWAY ROAD,
LONDON, N.7.

[*Received, February 21st*, 1958.]

[2] von Auwers and Beyhan, *J. prakt. Chem.*, 1935, **143**, 259.
[3] Claisen and Beyer, *Ber.*, 1887, **20**, 2186.
[4] von Auwers and Ungemach, *Ber.*, 1933, **66**, 1208.
[5] Brain and Finar, *J.*, 1957, 2356.

XUM

THE CHEMICAL SOCIETY

PATRON

HER MAJESTY THE QUEEN

President

H. J. Emeléus, C.B.E., M.A., D.Sc., F.R.S.

Vice-Presidents

who have filled the office of President

Sir Ian Heilbron, D.S.O., D.Sc., LL.D., F.R.S.
Sir Cyril Hinshelwood, M.A., Sc.D., F.R.S.
E. L. Hirst, C.B.E., D.Sc., LL.D., F.R.S.
Sir Christopher Ingold, D.Sc., F.R.I.C., F.R.S.
Sir Eric Rideal, M.B.E., M.A., D.Sc., F.R.S.
W. Wardlaw, C.B.E., D.Sc., F.R.I.C.

Vice-Presidents

Wilson Baker, M.A., D.Sc., F.R.S.
R. P. Bell, M.A., F.R.S.
R. D. Haworth, D.Sc., Ph.D., F.R.S.
E. D. Hughes, D.Sc., F.R.I.C., F.R.S.
F. G. Mann, Sc.D., D.Sc., F.R.S.
L. E. Sutton, M.A., D.Phil., F.R.S.

Honorary Treasurer

M. W. Perrin, C.B.E., M.A., F.R.I.C.

Honorary Secretaries

J. Chatt, M.A., Sc.D., F.R.I.C.
M. J. S. Dewar, M.A., D.Phil.
A. W. Johnson, Sc.D., Ph.D., A.R.C.S.

Ordinary Members of Council

R. G. R. Bacon, Ph.D., A.R.C.S.
R. M. Barrer, D.Sc., Sc.D., F.R.S.
A. J. Birch, M.Sc., D.Phil., F.R.S.
R. C. Cookson, M.A., Ph.D.
A. G. Evans, Ph.D., D.Sc., F.R.I.C.
A. C. Farthing, M.A., B.Sc., A.R.I.C.
R. H. Hall, Ph.D., A.R.C.S., F.R.I.C.
B. A. Hems, D.Sc., F.R.I.C.
L. Hunter, Ph.D., D.Sc., F.R.I.C.
L. H. Long, Ph.D., A.R.C.S., D.I.C.
J. D. Loudon, Ph.D., D.Sc.
B. Lythgoe, Ph.D., F.R.I.C., F.R.S.
A. Maccoll, M.Sc., Ph.D.
R. S. Nyholm, D.Sc., F.R.I.C., F.R.S.
R. E. Richards, M.A., D.Phil.
L. A. K. Staveley, M.A.
J. C. Tatlow, Ph.D., D.Sc., F.R.I.C.
R. H. Thomson, D.Sc., Ph.D., F.R.I.C.
A. I. Vogel, D.Sc., D.I.C., F.R.I.C.
W. B. Whalley, D.Sc., Ph.D., F.R.I.C.

General Secretary

J. R. Ruck Keene, M.B.E., T.D., M.A.

Librarian

R. G. Griffin, F.L.A.

Deputy Librarian

J. Bird

XUM

Recent Aspects of the Inorganic Chemistry of Nitrogen

THIS report of a Symposium held at Cambridge in 1957 has been issued as No. 10 in the Society's series of ' Special Publications '.

The contributors include C. C. Addison and B. J. Hathaway (Nottingham), L. G. Bartha and Z. G. Szabo (Szeged), L. Batt with B. G. Gowenlock and J. Trotman (Birmingham), Professor Dr Margot Becke-Goehring (Heidelberg), C. A. Bunton with D. R. Llewellyn and G. Stedman (London), G. Hetherington and P. L. Robinson (Durham), W. C. E. Higginson (Manchester), J. Jander with E. Kurzbach and E. Schmid (Freiburg), J. Lewis and D. B. Sowerby (Sheffield), R. E. Richards (Oxford), F. Seel (Würzburg), D. A. Spratt (I.C.I., Billingham).

Price: £1 5*s.* 0*d.*

THE CHEMICAL SOCIETY
BURLINGTON HOUSE, LONDON, W.1

Printed in Great Britain by Richard Clay and Company, Ltd., Bungay, Suffolk.

XUM

XUM